Hines
09/600398

FILE 'REGISTRY' ENTERED AT 10:45:32 ON 29 OCT 2001
E ADENYLATE KINASE/CN 5
L1 48 S ADENYLATE KINASE ?/CN

- key terms

FILE 'CAPLUS' ENTERED AT 10:46:23 ON 29 OCT 2001
L1 48 SEA FILE=REGISTRY ABB=ON PLU=ON ADENYLATE KINASE ?/CN
L2 990 SEA FILE=CAPLUS ABB=ON PLU=ON (L1 OR ADENYLATE KINASE) AND (DETERM? OR DETECT? OR DET## OR SCREEN? OR ASSAY?)
L3 75 SEA FILE=CAPLUS ABB=ON PLU=ON L2 AND BACTERI##
L4 7 SEA FILE=CAPLUS ABB=ON PLU=ON L3 AND (LYTIC OR LYS!S OR BACTERIOPHAGE)

L1 48 SEA FILE=REGISTRY ABB=ON PLU=ON ADENYLATE KINASE ?/CN
L5 11 SEA FILE=CAPLUS ABB=ON PLU=ON (L1 OR ADENYLATE KINASE) AND ANTIBIOT?

L6 17 L4 OR L5

L6 ANSWER 1 OF 17 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 2001:713538 CAPLUS
TITLE: Identification of essential genes in prokaryotes and use of their antisense constructs in antibiotic screening
INVENTOR(S): Haselbeck, Robert; Ohlsen, Kari L.; Zyskind, Judith W.; Wall, Daniel; Trawick, John D.; Carr, Grant J.; Yamamoto, Robert T.; Xu, H. Howard
PATENT ASSIGNEE(S): Elitra Pharmaceuticals, Inc., USA
SOURCE: PCT Int. Appl., 511 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001070955	A2	20010927	WO 2001-US9180	20010321

W: AE, AG, AL, AM, AT, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, CZ, DE, DE, DK, DK, DM, DZ, EE, EE, ES, FI, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.:
US 2000-191078 P 20000321
US 2000-206848 P 20000523
US 2000-207727 P 20000526
US 2000-242578 P 20001023
US 2000-253625 P 20001127
US 2000-257931 P 20001222
US 2001-269308 P 20010216

AB Genes required for proliferation of Staphylococcus aureus,

Salmonella typhimurium, Klebsiella pneumoniae, Pseudomonas aeruginosa, and Enterococcus faecalis. Libraries of genomic fragments were operably cloned into vectors comprising inducible promoters in the antisense orientation, and selected for those genes which which fail to grow or grow at a substantially reduced rate when the promoter is induced. The sequences of antisense nucleic acids which inhibit the proliferation of prokaryotes are disclosed. Cell-based assays which employ the antisense nucleic acids to identify and develop antibiotics are also disclosed. The antisense nucleic acids can also be used to identify proteins required for proliferation, express these proteins or portions thereof, obtain antibodies capable of specifically binding to the expressed proteins, and to use those expressed proteins as a screen to isolate candidate mols. for rational drug discovery programs. The nucleic acids can also be used to screen for homologous nucleic acids that are required for proliferation in cells other than Staphylococcus aureus, Salmonella typhimurium, Klebsiella pneumoniae, and Pseudomonas aeruginosa. The nucleic acids of the present invention can also be used in various assay systems to screen for proliferation required genes in other organisms.

IT INDEXING IN PROGRESS

L6 ANSWER 2 OF 17 CAPLUS COPYRIGHT 2001 ACS

ACCESSION NUMBER: 2001:384683 CAPLUS
DOCUMENT NUMBER: 135:1095
TITLE: Whole genome sequencing of meticillin-resistant Staphylococcus aureus
AUTHOR(S): Kuroda, Makoto; Ohta, Toshiko; Uchiyama, Ikuo; Baba, Tadashi; Yuzawa, Harumi; Kobayashi, Ichizo; Cui, Longzhu; Oguchi, Akio; Aoki, Ken-ichi; Nagai, Yoshimi; Lian, JianQi; Ito, Teruyo; Kanamori, Mutsumi; Matsumaru, Hiroyuki; Maruyama, Atsushi; Murakami, Hiroyuki; Hosoyama, Akira; Mizutani-Ui, Yoko; Takahashi, Noriko K.; Sawano, Toshihiko; Inoue, Ryu-ichi; Kaito, Chikara; Sekimizu, Kazuhisa; Hirakawa, Hideki; Kuhara, Satoru; Goto, Susumu; Yabuzaki, Junko; Kanehisa, Minoru; Yamashita, Atsushi; Oshima, Kenshiro; Furuya, Keiko; Yoshino, Chie; Shiba, Tadayoshi; Hattori, Masahira; Ogasawara, Naotake; Hayashi, Hideo; Hiramatsu, Keiichi
CORPORATE SOURCE: Department of Bacterlology, Juntendo University, Tokyo, 113 8421, Japan
SOURCE: Lancet (2001), 357(9264), 1225-1240
CODEN: LANCAO; ISSN: 0140-6736
PUBLISHER: Lancet Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Staphylococcus aureus is one of the major causes of community-acquired and hospital-acquired infections. It produces numerous toxins including superantigens that cause unique disease entities such as toxic-shock syndrome and staphylococcal scarlet fever, and has acquired resistance to practically all **antibiotics**. Whole genome anal. is a necessary step towards future development of countermeasures against this organism. Whole genome sequences of two related S aureus strains (N315 and Mu50) were detd. by shot-gun random sequencing. N315 is a meticillin-resistant S aureus (MRSA) strain isolated in 1982, and

Mu50 is an MRSA strain with vancomycin resistance isolated in 1997. The open reading frames were identified by use of GAMBLER and GLIMMER programs, and annotation of each was done with a BLAST homol. search, motif anal., and protein localization prediction. The Staphylococcus genome was composed of a complex mixt. of genes, many of which seem to have been acquired by lateral gene transfer. Most of the **antibiotic** resistance genes were carried either by plasmids or by mobile genetic elements including a unique resistance island. Three classes of new pathogenicity islands were identified in the genome: a toxic shock syndrome toxin island family, exotoxin islands, and enterotoxin islands. In the latter two pathogenicity islands, clusters of exotoxin and enterotoxin genes were found closely linked with other gene clusters encoding putative pathogenic factors. The anal. also identified 70 candidates for new virulence factors. The remarkable ability of S aureus to acquire useful genes from various organisms was revealed through the observation of genome complexity and evidence of lateral gene transfer. Repeated duplication of genes encoding superantigens explains why S aureus is capable of infecting humans of diverse genetic backgrounds, eliciting severe immune reactions. Investigation of many newly identified gene products, including the 70 putative virulence factors, will greatly improve our understanding of the biol. of staphylococci and the processes of infectious diseases caused by S aureus.

IT **341086-64-4**
RL: BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)
(amino acid sequence; whole genome sequencing of meticillin-resistant Staphylococcus aureus)

REFERENCE COUNT: 43
REFERENCE(S):
(1) Abe, J; Proc Natl Acad Sci 1992, V89, P4066 CAPLUS
(2) Agata, N; Microbiology 1995, V141, P983 CAPLUS
(3) Alm, R; Nature 1999, V397, P176 CAPLUS
(5) Bissett, D; J Bacteriol 1974, V119, P698 CAPLUS
(6) Blattner, F; Science 1997, V277, P1453 CAPLUS
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 3 OF 17 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 2001:302411 CAPLUS
DOCUMENT NUMBER: 134:306044
TITLE: Complete genome sequence of an M1 strain of Streptococcus pyogenes
AUTHOR(S): Ferretti, Joseph J.; McShan, William M.; Ajdic, Dragana; Savic, Dragutin J.; Savic, Gorana; Lyon, Kevin; Primeaux, Charles; Sezate, Steven; Suvorov, Alexander N.; Kenton, Steve; Lai, Hong Shing; Lin, Shao Ping; Qian, Yudong; Jia, Hong Gui; Najar, Fares Z.; Ren, Qun; Zhu, Hua; Song, Lin; White, Jim; Yuan, Xiling; Clifton, Sandra W.; Roe, Bruce A.; McLaughlin, Robert
CORPORATE SOURCE: Department of Microbiology and Immunology, University of Oklahoma Health Sciences Center, Oklahoma City, OK, 73190, USA
SOURCE: Proc. Natl. Acad. Sci. U. S. A. (2001), 98(8),

4658-4663
CODEN: PNASA6; ISSN: 0027-8424
PUBLISHER: National Academy of Sciences
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The 1,852,442-bp sequence of an M1 strain of Streptococcus pyogenes, a Gram-pos. pathogen, was **detd.** and contains 1752 predicted protein-encoding genes. Approx. one-third of these genes have no identifiable function, with the remainder falling into previously characterized categories of known microbial function. Consistent with the observation that S. pyogenes is responsible for a wider variety of human disease than any other **bacterial** species, >40 putative virulence-assocd. genes were identified. Addnl. genes were identified that encode proteins likely assocd. with microbial "mol. mimicry" of host characteristics and involved in rheumatic fever or acute glomerulonephritis. The complete or partial sequence of 4 different **bacteriophage** genomes is also present, with each contg. genes for one or more previously undiscovered superantigen-like proteins. These prophage-assocd. genes encode at least 6 potential virulence factors, emphasizing the importance of **bacteriophages** in horizontal gene transfer and a possible mechanism for generating new strains with increased pathogenic potential.

IT **334848-07-6**
RL: BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)
(amino acid sequence; complete genome sequence of an M1 strain of Streptococcus pyogenes)

REFERENCE COUNT: 56
REFERENCE(S):
(1) Bateman, A; Nucleic Acids Res 2000, V28, P263 CAPLUS
(2) Bender, G; Infect Immun 1986, V53, P331 CAPLUS
(3) Berge, A; Infect Immun 1998, V66, P3449 CAPLUS
(4) Bernish, B; J Biol Chem 1999, V274, P4786 CAPLUS
(5) Bessen, D; J Exp Med 1990, V172, P1757 CAPLUS
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 4 OF 17 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 2001:98372 CAPLUS
DOCUMENT NUMBER: 134:232542
TITLE: Genome sequence of enterohemorrhagic Escherichia coli O157:H7
AUTHOR(S): Perna, Nicole T.; Plunkett, Guy, III; Burland, Valerie; Mau, Bob; Glasner, Jeremy D.; Rose, Debra J.; Mayhew, George F.; Evans, Peter S.; Gregor, Jason; Kirkpatrick, Heather A.; Posfai, Gyorgy; Hackett, Jeremiah; Klink, Sara; Boutin, Adam; Shao, Ying; Miller, Leslie; Grotbeck, Erik J.; Davis, N. Wayne; Lim, Alex; Dimalanta, Eileen T.; Potamousis, Konstantinos D.; Apodaca, Jennifer; Anantharaman, Thomas S.; Lin, Jieyi; Yen, Glaex; Schwartz, David C.; Welch, Rodney A.; Blattner, Frederick R.
CORPORATE SOURCE: Genome Center of Wisconsin, Department of Animal

Health and Biomedical Sciences, Laboratory of Genetics, Department of Chemistry, Department of Biostatistics, and Department of Medical Microbiology and Immunology, University of Wisconsin, Madison, WI, 53706, USA
SOURCE: Nature (London) (2001), 409(6819), 529-533
CODEN: NATUAS; ISSN: 0028-0836
PUBLISHER: Nature Publishing Group
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The **bacterium** Escherichia coli O157:H7 is a worldwide threat to public health and has been implicated in many outbreaks of hemorrhagic colitis, some of which included fatalities caused by hemolytic uremic syndrome. Close to 75,000 cases of O157:H7 infection are now estd. to occur annually in the United States. The severity of disease, the lack of effective treatment and the potential for large-scale outbreaks from contaminated food supplies have propelled intensive research on the pathogenesis and **detection** of E. coli O157:H7. The genome of E. coli O157:H7 was sequenced to identify candidate genes responsible for pathogenesis, to develop better methods of strain **detection** and to advance our understanding of the evolution of E. coli, through comparison with the genome of the non-pathogenic lab. strain E. coli K-12. Lateral gene transfer found to be far more extensive than previously anticipated. In fact, 1387 new genes encoded in strain-specific clusters of diverse sizes were found in O157:H7. These include candidate virulence factors, alternative metabolic capacities, several prophages, and other new functions - all of which could be targets for surveillance.
IT **197181-09-2**
RL: BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)
(amino acid sequence; genome sequence of enterohemorrhagic Escherichia coli O157,H7)
REFERENCE COUNT: 30
REFERENCE(S):
(1) Alm, R; J Mol Med 1999, V77, P834 CAPLUS
(2) Altschul, S; J Mol Biol 1990, V215, P403 CAPLUS
(3) Blaisdell, J; J Bacteriol 1999, V181, P6396 CAPLUS
(5) Blattner, F; Science 1997, V277, P1453 CAPLUS
(6) Boyd, E; J Bacteriol 1997, V179, P1985 CAPLUS
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 5 OF 17 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 2000:636908 CAPLUS
DOCUMENT NUMBER: 133:262066
TITLE: Complete genome sequence of Pseudomonas aeruginosa PA01
AUTHOR(S): Stover, C. K.; Pham, X. Q.; Erwin, A. L.; Mizoguchi, S. D.; Warrener, P.; Hickey, M. J.; Brinkman, F. S. L.; Hufnagle, W. O.; Kowalik, J.; Lagrou, M.; Garber, R. L.; Goltry, L.; Tolentino, E.; Westbrock-Wadman, S.; Yuan, Y.; Brody, L. L.; Coulter, S. N.; Folger, K. R.; Kas, A.; Larbig, K.; Lim, R.; Smith, K.;

Spencer, D.; Wong, G. K.-S.; Wu, Z.; Paulsen, I. T.; Reizer, J.; Saier, M. H.; Hancock, R. E. W.; Lory, S.; Olson, M. V.

CORPORATE SOURCE: PathoGenesis Corporation, Seattle, WA, 98119, USA

SOURCE: Nature (London) (2000), 406(6799), 959-964
CODEN: NATUAS; ISSN: 0028-0836
PUBLISHER: Nature Publishing Group
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Pseudomonas aeruginosa is a ubiquitous environmental bacterium that is one of the top three causes of opportunistic human infections. A major factor in its prominence as a pathogen is its intrinsic resistance to **antibiotics** and disinfectants. The authors now report the complete sequence of P. aeruginosa strain PA01. At 6.3 million base pairs, this is the largest bacterial genome sequenced, and the sequence provides insights into the basis of the versatility and intrinsic drug resistance of P. aeruginosa. Consistent with its larger genome size and environmental adaptability, P. aeruginosa contains the highest proportion of regulatory genes obsd. for a bacterial genome and a large no. of genes involved in the catabolism, transport and efflux of org. compds. as well as four potential chemotaxis systems. The size and complexity of the P. aeruginosa genome is proposed to reflect an evolutionary adaptation permitting it to thrive in diverse environments and resist the effects of a variety of antimicrobial substances. The genome and protein sequences are deposited in the GenBank database with Accession No. AE004091, as well at the web site http://www.pseudomonas.com. .

IT **297316-80-4**
RL: BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)
(amino acid sequence; complete genome sequence of Pseudomonas aeruginosa PA01)

REFERENCE COUNT: 44
REFERENCE(S):
(2) Altschul, S; Nucleic Acids Res 1997, V25, P3389 CAPLUS
(3) Armitage, J; Microbiology 1997, V143, P3671 CAPLUS
(4) Ball, C; Nucleic Acids Res 2000, V28, P77 CAPLUS
(6) Blattner, F; Science 1997, V277, P1453 CAPLUS
(7) Bleves, S; J Bacteriol 1999, V181, P4012 CAPLUS
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 6 OF 17 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 2000:540554 CAPLUS
DOCUMENT NUMBER: 133:130477
TITLE: The genome sequence of the plant pathogen Xylella fastidiosa
AUTHOR(S): Simpson, A. J. G.; Reinach, F. C.; Arruda, P.; Abreu, F. A.; Acencio, M.; Alvarenga, R.; Alves, L. M. C.; Araya, J. E.; Bala, G. S.; Baptista, C. S.; Barros, M. H.; Bonaccorsi, E. D.; Bordin, S.; Bove, J. M.; Briones, M. R. S.; Bueno, M. R. P.; Camargo, A. A.; Camargo, L. E. A.; Carraro,

D. M.; Carrer, H.; Colauto, N. B.; Colombo, C.; Costa, F. F.; Costa, M. C. R.; Costa-Neto, C. M.; Coutinho, L. L.; Cristofani, M.; Dias-Neto, E.; Docena, C.; El-Dorry, H.; Facincani, A. P.; Ferreira, A. J. S.; Ferreira, V. C. A.; Ferro, J. A.; Fraga, J. S.; Franca, S. C.; Franco, M. C.; Frohme, M.; Furtan, L. R.; Garnier, M.; Goldman, G. H.; Goldman, M. H. S.; Gomes, S. L.; Gruber, A.; Ho, P. L.; Hoheisel, J. D.; Junqueira, M. L.; Kemper, E. L.; Kitajima, J. P.; Kreiger, J. E.; Duramae, E. E.; Laigret, F.; Lambals, M. R.; Lette, L. C. C.; Lemos, E. G. M.; Lemos, M. V. F.; Lopes, S. A.; Lopes, C. R.; Machado, J. A.; et al.

CORPORATE SOURCE: Instituo Ludwig de Pesquisa sobre o Cancer, Sao Paulo, 01509-010, Brazil

SOURCE: Nature (London) (2000), 406(6792), 151-157
CODEN: NATUAS; ISSN: 0028-0836

PUBLISHER: Nature Publishing Group
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Xylella fastidiosa is a fastidious, xylem-limited bacterium that causes a range of economically important plant diseases. The complete genome sequence of X. fastidiosa clone 9a5c, which causes citrus variegated chlorosis-a serious disease of orange trees, is reported. The genome comprises a 52.7% GC-rich 2,679,305-base-pair (bp) circular chromosome and two plasmids of 51,158 bp and 1,285 bp. Putative functions can be assigned to 47% of the 2904 predicted coding regions. Efficient metabolic functions are predicted, with sugars as the principal energy and carbon source, supporting existence in the nutrient-poor xylem sap. The mechanisms assocd. with pathogenicity and virulence involve toxins, **antibiotics** and ion sequestration systems, as well as bacterium-bacterium and bacterium-host interactions mediated by a range of proteins. Orthologs of some of these proteins have only been identified in animal and human pathogens; their presence in X. fastidiosa indicates that the mol. basis for bacterial pathogenicity is both conserved and independent of host. At least 83 genes are bacteriophage-derived and include virulence-assocd. genes from other bacteria, providing direct evidence of phage-mediated horizontal gene transfer.

IT **284694-29-7**
RL: BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)
(amino acid sequence; genome sequence of the plant pathogen Xylella fastidiosa)

L6 ANSWER 7 OF 17 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1999:496888 CAPLUS
DOCUMENT NUMBER: 132:75617
TITLE: **Antibiotic** sensitivity testing using bacteriophage mediated lysis and ak bioluminescence
AUTHOR(S): Price, R. L.; Murphy, M. J.; Squirrell, D. J.
CORPORATE SOURCE: DERA Porton Down, Salisbury, Wiltshire, SP4 0JQ, UK
SOURCE: Biolumin. Chemilumin., Proc. Int. Symp., 10th (1999), Meeting Date 1998, 173-176. Editor(s):

Roda, Aldo. Wiley: Chichester, UK.
CODEN: 67YCAD
DOCUMENT TYPE: Conference
LANGUAGE: English
AB A rapid method for detn. the resistance or susceptibility to **antibiotics** of an E. coli strain in pure culture has been demonstrated. The model system based on pure culture was used for simplicity but the authors believe that this technique could have enormous potential when fully developed.
REFERENCE COUNT: 5
REFERENCE(S):
(1) Blasco, R; Journal of Applied Microbiology 1998, V84, P661 CAPLUS
(2) Hugo, W; Pharmaceutical Microbiology 5th edition 1992
(3) Madigan, M; Brock Biology of Microorganisms 8th edition 1997
(4) Sanders, M; Bioluminescence and Chemiluminescence: Fundamentals and Applied Aspects 1994, P454 CAPLUS
(5) Squirrell, D; Bioluminescence and Chemiluminescence: Fundamentals and Applied Aspects 1994, P486 CAPLUS

L6 ANSWER 8 OF 17 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1999:487415 CAPLUS
DOCUMENT NUMBER: 131:99528
TITLE: **Antibiotic** sensitivity testing
INVENTOR(S): Murphy, Melanie Jane; Price, Rachel Louise; Squirrell, David James
PATENT ASSIGNEE(S): The Secretary of State for Defence, UK
SOURCE: PCT Int. Appl., 36 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9937799	A1	19990729	WO 1999-GB89	19990112
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
AU 9920653	A1	19990809	AU 1999-20653	19990112
GB 2348702	A1	20001011	GB 2000-20001729	19990112
BR 9907161	A	20001024	BR 1999-7161	19990112
EP 1049798	A1	20001108	EP 1999-901020	19990112
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE				
NO 2000003708	A	20000921	NO 2000-3708	20000719

PRIORITY APPLN. INFO.: GB 1998-1126 A 19980121
GB 1998-16993 A 19980806

WO 1999-GB89 W 19990112

AB The use of an **assay** for **adenylate kinase** in an in vitro test for the effect of external conditions on the growth characteristics of **bacterial** cells. Such tests in particular include tests for the sensitivity of a **bacteria** to an **antibiotic** or a biostatic agent, and tests to assess the growth stage and health of the **bacteria**. Methods of carrying out these tests and kits for effecting them are also described and claimed.

REFERENCE COUNT: 8

REFERENCE(S):
(1) Blasco, R; J APPL MICROBIOL 1998, V84(4), P661 CAPLUS
(3) James, S; WO 9417202 A 1994 CAPLUS
(4) James, S; WO 9602665 A 1996 CAPLUS
(5) Mercian Corp; JP 04370100 A 1992 CAPLUS
(7) Secr Defence; WO 9602666 A 1996 CAPLUS
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 9 OF 17 CAPLUS COPYRIGHT 2001 ACS

ACCESSION NUMBER: 1999:299524 CAPLUS
DOCUMENT NUMBER: 130:307540
TITLE: Production of the **adenylate kinase** free luciferase using recombinant Escherichia coli expression system
INVENTOR(S): Squirrell, David James; Price, Rachel Louise; Murphy, Melanie Jane
PATENT ASSIGNEE(S): The Secretary of State for Defence, UK
SOURCE: PCT Int. Appl., 15 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9922004	A1	19990506	WO 1998-GB3034	19981009
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW				
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
AU 9893600	A1	19990517	AU 1998-93600	19981009
AU 731446	B2	20010329		
EP 1025235	A1	20000809	EP 1998-946599	19981009
R: AT, BE, CH, DE, DK, ES, FR, GB, IT, LI, LU, NL, SE, PT, IE, FI				

PRIORITY APPLN. INFO.: GB 1997-22481 A 19971025
WO 1998-GB3034 W 19981009

AB **Adenylate kinase** contamination of luciferase can lead to false-pos. signals when the enzyme is used anal. A method for producing luciferase which is substantially free of **adenylate kinase** is described. In this method substitution mutations were introduced into the E. coli **adenylate kinase** gene to generate a thermolabile kinase that was unstable at .gtoreq. 37.degree.. A plasmid bearing

the gene for a thermostable luciferase was then introduced into this host such that the luciferase could be produced at a temp. that is permissive to the **adenylate kinase**. The culture then was raised to a higher temp. to denature the **adenylate kinase** which was present. The method can be generally applied to the prodn. of polypeptides free of specific contaminants.

REFERENCE COUNT: 4
REFERENCE(S):
(1) Belinga, H; J Chromatogr 1995, V695(1), P33 CAPLUS
(2) Nasoff, M; US 5030563 A 1991 CAPLUS
(3) Squirrell, D; WO 9417202 A 1994 CAPLUS
(4) Squirrell, D; WO 9622376 A 1996 CAPLUS

L6 ANSWER 10 OF 17 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1998:368650 CAPLUS
DOCUMENT NUMBER: 129:146444
TITLE: Specific **assays** for **bacteria** using phage mediated release of **adenylate kinase**
AUTHOR(S): Blasco, R.; Murphy, M. J.; Sanders, M. F.; Squirrell, D. J.
CORPORATE SOURCE: MAFF Central Science Laboratory, York, UK
SOURCE: J. Appl. Microbiol. (1998), 84(4), 661-666 CODEN: JAMIFK; ISSN: 1364-5072
PUBLISHER: Blackwell Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB A sensitive and rapid **assay** method for the specific **detection** of **bacteria** was developed using Escherichia coli and Salmonella newport as the test organisms. **Bacteriophages** were used to provide specific **lysis** of the **bacteria** and then the release of cell contents was measured by ATP bioluminescence. Increased sensitivity was obtained by focusing on the **bacteria's adenylate kinase** (AK) as the cell marker instead of ATP as conventionally used. Fewer than 103 E. coli cells could be readily **detected** in less than 1 h. Salmonella newport **assays**, although as sensitive, were slower and took up to 2 h. The effects of the culture medium, the phage, and the presence of non-specific **bacteria** were examd.

L6 ANSWER 11 OF 17 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1997:748948 CAPLUS
DOCUMENT NUMBER: 128:150233
TITLE: The complete genome sequence of the gram-positive bacterium Bacillus subtilis
AUTHOR(S): Kunst, F.; Ogasawara, N.; Moszer, I.; Albertini, A. M.; Alloni, G.; Azevedo, V.; Bertero, M. G.; Bessieres, P.; Bolotin, A.; Borchert, S.; Borriss, R.; Boursier, L.; Brans, A.; Braun, M.; Brignell, S. C.; Bron, S.; Brouillet, S.; Bruschi, C. V.; Caldwell, B.; Capuano, V.; Carter, N. M.; Choi, S.-K.; Codani, J.-J.; Connerton, I. F.; Cummings, N. J.; Daniel, R. A.; Denizot, F.; Devine, K. M.; Dusterhoft, A.; Ehrlich, S. D.; Emmerson, P. T.; Entian, K. D.; Errington, J.; Fabret, C.; Ferrari, E.; Foulger, D.; Fritz, C.; Fujita, M.; Fujita, Y.; Fuma, S.;

Galizzi, A.; Galleron, N.; Ghim, S.-Y.; Glaser, P.; Goffeau, A.; Golightly, E. J.; Grandi, G.; Guiseppi, G.; Guy, B. J.; Haga, K.; et al.
CORPORATE SOURCE: Unite de Biochemie Microbienne, Inst. Pasteur, Paris, 75724, Fr.
SOURCE: Nature (London) (1997), 390(6657), 249-256
CODEN: NATUAS; ISSN: 0028-0836
PUBLISHER: Macmillan Magazines
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Bacillus subtilis is the best-characterized member of the gram-pos. bacteria. Its genome of 4,214,810 base pairs comprises 4100 protein-coding genes. Of these protein-coding genes, 53% are represented once, while a quarter of the genome corresponds to several gene families that have been greatly expanded by gene duplication, the largest family contg. 77 putative ATP-binding transport proteins. In addn., a large proportion of the genetic capacity is devoted to the utilization of a variety of carbon sources, including many plant-derived mols. The identification of 5 signal peptidase genes, as well as several genes for components of the secretion app., is important given the capacity of Bacillus strains to secrete large amts. of industrially important enzymes. Many of the genes are involved in the synthesis of secondary metabolites, including **antibiotics**, that are more typically assocd. with Streptomyces species. The genome contains .gtoreq.10 prophages or remnants of prophages, indicating that bacteriophage infection has played an important evolutionary role in horizontal gene transfer, in particular in the propagation of bacterial pathogenesis.
IT **128512-97-0**
RL: PRP (Properties)
(amino acid sequence; complete genome sequence of Bacillus subtilis)

L6 ANSWER 12 OF 17 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1995:943660 CAPLUS
DOCUMENT NUMBER: 123:332582
TITLE: Cellular material **detection** apparatus and method
INVENTOR(S): Squirrell, David James
PATENT ASSIGNEE(S): United Kingdom Secretary of State for Defence, London, UK
SOURCE: PCT Int. Appl., 32 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9525811	A1	19950928	WO 1995-GB544	19950313

W: AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, JP, KE, KG, KP, KR, KZ, LK, LR, LT, LU, LV, MD, MG, MN, MW, MX, NL, NO, NZ, PL, PT, RO, RU, SD, SE, SI, SK, TJ, TT, UA, US
RW: KE, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML,

MR, NE, SN, TD, TG

CA 2195956	AA	19950928	CA 1995-2195956	19950313	
AU 9518588	A1	19951009	AU 1995-18588	19950313	
AU 699575	B2	19981210			
EP 789778	A1	19970820	EP 1995-910682	19950313	
EP 789778	B1	20010530			
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, NL, PT, SE					
RU 2142016	C1	19991127	RU 1997-106556	19950313	
ES 2156937	T3	20010801	ES 1995-910682	19950313	
US 5773710	A	19980630	US 1997-793011	19970205	
US 5918259	A	19990629	US 1998-63368	19980421	

PRIORITY APPLN. INFO.:	GB 1994-5392	A	19940318
	WO 1995-GB544	W	19950313
	US 1997-793011	A3	19970205

AB A method and app. for monitoring a gaseous environment for the presence of cellular material; more particularly an app. and method that is capable of providing a measure of presence and/or nos. of cellular microorganisms, such as **bacterial** cells, in a large vol. of air such as in a warehouse or prodn. facility or in an open air location where **bacterial** presence is suspected. The method and app. of the invention are particularly provided for **detg.** the likelihood of pathogenic material being present in an environment by batch or online measurement of cell nos. In the latter format, a continuous monitoring of an environment for presence of pathogens is effected. The app. comprises a continuous flow luminometer preferably fed by a cyclone or high velocity virtual impactor and **lytic** and luminescence reagents which **detect** the amt. of ATP or **adenylate kinase** present in a sample of air.

L6 ANSWER 13 OF 17 CAPLUS COPYRIGHT 2001 ACS

ACCESSION NUMBER:	1995:817454 CAPLUS
DOCUMENT NUMBER:	124:2036
TITLE:	A novel locus of Yersinia enterocolitica serotype O:3 involved in lipopolysaccharide outer core biosynthesis
AUTHOR(S):	Skurnik, Mikael; Venho, Reija; Toivanen, Paavo; Al-Hendy, Ayman
CORPORATE SOURCE:	Turku Centre Biotechnology and Department of Medical Microbiology, University of Turku, Turku, FIN-20520, Finland
SOURCE:	Mol. Microbiol. (1995), 17(3), 575-94 CODEN: MOMIEE; ISSN: 0950-382X
DOCUMENT TYPE:	Journal
LANGUAGE:	English

AB Yersinia enterocolicita serotype O:3 strain 6471/76-c (YeO3-c) was sensitive to **bacteriophage** .vphi.R1-37 when grown at 37.degree.C but not when grown at 22.degree.C because of steric hindrance by abundantly lipopolysaccharide (LPS) O-side chain (O-antigen) expressed at 22.degree.C. The transposon library of YeO3-c was grown at 37.degree.C and **screened** for phage .vphi.R1-37-resistant transposon insertion mutants. Three types of mutant were isolated: (i) phage receptor mutants expressing O-antigen (LPS-smooth), (ii) phage receptor mutants not expressing O-antigen (LPS-rough), and (iii) LPS-smooth mutants with the phage receptor constitutively sterically blocked. Mutant type (i) was characterized in detail; the transposon insertion inactivates an

operon, named the trs operon. The main findings based on this mutant are: (i) the trs operon is involved in the biosynthesis of the of the LPS outer core in YeO3-c; the nucleotide sequence of the trs operon revealed eight novel genes showing similarity to known polysaccharide biosynthetic genes of various Gram-neg. **bacteria** as well as to capsule biosynthesis gene of Staphylococcus aureus; (ii) the biosynthesis of thee coree of YeO3-c involves at least two genetic loci; (iii) the trs operon is required for the biosynthesis of the **bacteriophage** .vphi.R1-37 receptor structures; (i.v.) the homopolymeric O-antigen of YeO3-c is ligated to the inner core in Y. enterocolitica O:3; (v) the trs operon is located between the adk-hemH and galE-gsk gene pairs in the Y. enterocolitica chromosome; and (vi) the phage .vphi.R1-37 receptor is present in many but not in all Y. enterocolitica serotypes. The results also allow us to speculate that the trs operon is a relic of the ancestral rfb region of Y. enterocolitica O:3 carrying genes indispensable for the completion of the core polysaccharide biosynthesis.

L6 ANSWER 14 OF 17 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1978:472160 CAPLUS
DOCUMENT NUMBER: 89:72160
TITLE: Effect of inducers of cation permeability on the binding of cytochrome c with the mitochondrial membrane
AUTHOR(S): Shol'ts, K. F.; Solov'eva, N. A.; Shul'gin, M. N.; Kotel'nikova, A. V.
CORPORATE SOURCE: A. N. Bakh Inst. Biochem., Moscow, USSR
SOURCE: Biokhimiya (Moscow) (1978), 43(6), 1012-18
CODEN: BIOHAO; ISSN: 0006-307X
DOCUMENT TYPE: Journal
LANGUAGE: Russian
AB The alkali cation permeability-inducers valinomycin, gramicidin A, and N,N'-diacetylgramicidin S at optimal concns. for uncoupling caused biphasic activation of rat liver mitochondrial respiration, and this effect resulted from cytochrome c solubilization. Gramicidin S at optimal uncoupling concns. did not solubilize cytochrome c from the respirating mitochondria. This property of gramicidin S is apparently due to cytochrome c immobilization in the membrane by this compd. **Adenylate kinase** was also released by the first 3 but not the last **antibiotic**.

L6 ANSWER 15 OF 17 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1975:574737 CAPLUS
DOCUMENT NUMBER: 83:174737
TITLE: Comparison of the predicted and observed secondary structure of T4 phage lysozyme
AUTHOR(S): Matthews, B. W.
CORPORATE SOURCE: Inst. Mol. Biol., Univ. Oregon, Eugene, Oreg., USA
SOURCE: Biochim. Biophys. Acta (1975), 405(2), 442-51
CODEN: BBACAQ
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Predictions of the secondary structure of T4 phage lysozyme, made by a no. of investigators on the basis of the amino acid sequence, are compared with the structure of the protein **detd.** exptl. by x-ray crystallog. Within the N-terminal half of the mol., the

locations of helices predicted by a no. of methods agree moderately well with the obsd. structure; however, within the C-terminal half of the mol., the overall agreement is poor. For 11 different helix predictions, the coeffs. giving the correlation between prediction and observation range from 0.14 to 0.42. The accuracy of the predictions for both .beta.-sheet regions and for turns are generally lower than for the helices, and in a no. of instances the agreement between prediction and observation is no better than would be expected for a random selection of residues. The structural predictions for T4 phage lysozyme are much less successful than was the case for **adenylate kinase** by G. E. Schulz et al. (1974). No one method of prediction is clearly superior to all others, and although empirical predictions based on larger nos. of known protein structure tend to be more accurate than those based on a limited sample, the improvement in accuracy is not dramatic, suggesting that the accuracy of current empirical predictive methods will not be substantially increased simply by the inclusion of more data from addnl. protein structure **detns**.

L6 ANSWER 16 OF 17 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1966:484809 CAPLUS
DOCUMENT NUMBER: 65:84809
ORIGINAL REFERENCE NO.: 65:15926g-h,15927a-c
TITLE: Mechanism of action of colchicine
AUTHOR(S): Chakraborty, Arun; Biswas, B. B.
CORPORATE SOURCE: Bose Inst., Calcutta
SOURCE: Bull. Botan. Soc. Bengal (1964), 18(1-2), 214-20
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Roots grown by germinating bulbs of Allium cepa on tap water for 48 hrs. at 20.degree. were cut 1.5-2 cm. from the tip and incubated after washing with glass distd. water. Tumors were obtained by dipping the tip portions of newly grown roots into 0.05% aq. solns. of colchicine for 46 hrs. The control plants were grown on water for the same time at the same temp. Marked antagonism against the tumor growth was exhibited by 0.01% ATP. No tumor formation occurred in the presence of actinomycin D, 0.005%, though the treatment with this **antibiotic** for a time longer than 36 hrs. resulted in the appearance of certain deformities. At 4% concn., EtOH overcame both the morphological defects of tumor formation and the halt in longitudinal growth. Chloramphenicol had no effect on tumor growth. In the total acid sol. fraction there was an increase in 32P incorporation in the colchicine-treated roots. The radioactivity in AMP, ADP, and ATP was considerably lower in the treated than in the control while just the reverse was the case with pyridine nucleotides. Though there was a decrease in the pool size of ATP in the cell due to colchicine treatment, the activity of **adenylate kinase** was the same in the control as in the treated. Uracil-14C incorporation into RNA, thymine-14C into DNA, and 32P into both were markedly increased in the treated roots. The decrease in the nucleotide pool was thus correlated with this increased synthesis. The RNA polymerase activity in the exts. of treated root tips was much higher than in the control and the RNA isolated from the treated root tips had increased AMP and UMP residues. The treated root tips incorporated more 14C-labeled amino acids into proteins than the control. The proteins of the root tips were extd. with 0.05M Tris, pH 7.5, 0.6M KCl, and 0.24N HCl and KOH stepwisely. In the treated samples,

incorporation of 14C-labeled amino acids increased by 37, 26, 22, and 172% in buffer-, KCl-, and HCl-sol. fractions, and residues, resp., with respect to the control samples. The unimpaired incorporation of labeled amino acids into the KCl-extd. fraction suggested that the colchicine probably did not inhibit the primary synthesis of the spindle protein. A comparison of the values of SH and SS in the buffer-extd. and KCl-extd. proteins indicated that the 2 groups of proteins were widely different in this respect. In the buffer-exts., SH content remained almost the same in the control and in the treated root tips. In the KCl-extd. proteins, free SH was reduced in the treated to about half of that of the control and this redn. in SH content was accompanied by a concomitant increase, .apprx.2-fold, in SS content. There was no appreciable change in the SS content of the control and treated buffer exts.

L6 ANSWER 17 OF 17 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1961:144668 CAPLUS
DOCUMENT NUMBER: 55:144668
ORIGINAL REFERENCE NO.: 55:27483e-i,27484a-b
TITLE: Properties of the inorganic orthophosphate-adenosine triphosphate and adenosine diphosphate-adenosine triphosphate exchange reactions of digitonin particles
AUTHOR(S): Cooper, Cecil; Kulka, Richard G.
CORPORATE SOURCE: Western Reserve Univ., Cleveland, OH
SOURCE: J. Biol. Chem. (1961), 236, 2351-6
DOCUMENT TYPE: Journal
LANGUAGE: Unavailable
AB cf. CA 55, 8848i. The properties were compared of the inorg. orthophosphate-adenosine triphosphate (ATP) and adenosine diphosphate (ADP)-ATP exchange reactions catalyzed by digitonin particles from rat-liver mitochondria. Both reactions are inhibited to the same extent by the following: aging at 0.degree. or 37.degree.; increasing the concn. of ADP from 4 .times. 10-4M to 0.005M; NaN3, sucrose, and AgNO3; and irradiation by near-ultraviolet light. They are both stimulated to the same degree by increasing the inorg. P concn. from 2 .times. 10-4M to 0.01M. From a comparison of the relative rates of the 2 reactions it appears that the ADP-ATP reaction is more rapid. This conclusion is uncertain owing to difficulties in evaluating **adenylate kinase** activity. Studies with the digitonin particles showed that the incorporation of P32 into the terminal P of ATP from ADP-P32 under conditions used to det. exchange is decreased 60-70% by 1.5 .times. 10-4M pentachlorophenol. Thus the value applied to the total observed ADP-ATP exchange to correct for **adenylate kinase** can be underestd. by as much as a factor of 3. All the proposed mechanisms for oxidative phosphorylation envisage a stepwise reaction of inorg. P and ADP. The data presented herein do not exclude such a reaction sequence but they are also in accord with a different mechanism, namely, the simultaneous reaction of inorg. P and ADP at a single enzymic site. Expts. were conducted with **adenylate kinase** prepd. from pig liver and rabbit muscle. The results are interpreted to mean that **adenylate kinase** itself cannot lead to an uneven isotope distribution and that the sol. enzyme probably contains one or more enzymes, insensitive to Ag, that catalyze an ADP-ATP exchange reaction. The results obtained with the same enzyme prepn. in the presence and absence of Mg are strikingly different. The

reaction proceeded to a much greater extent in the presence of Mg than in its absence. In the absence of Mg, the **adenylate kinase** measured with ADP-P32 alone or with AMP-8-C14 plus ATP is greater than the isotope incorporation detd. with ADP-P32 plus ATP. In the presence of Mg the reverse occurs. A sol. ext. was prepd. from an acetone powder of digitonin particles which catalyzes an ADP-ATP exchange that is largely insensitive to pentachlorophenol. It is suggested that a considerable portion of this exchange activity is due to **adenylate kinase** . The effect was examd. of oligomycin on the exchange reactions catalyzed by digitonin particles. Both the inorg.-ATP exchange and the portion of the ADP-ATP exchange sensitive to pentachlorophenol underwent a parallel, progressive inhibition in the presence of increasing amts. of the **antibiotic**. A 50% inhibition of both reactions is produced by 0.11-0.14 .gamma. of oligomycin/0.3 mg. of particle protein/ml.

(FILE 'CAPLUS' ENTERED AT 10:46:23 ON 29 OCT 2001)

L7 1193 SEA ABB=ON PLU=ON (L1 OR (MYO OR ADENYLATE)(W)KINASE OR MYOKINASE) AND (DETERM? OR DETECT? OR DET## OR SCREEN? OR ASSAY?)
L8 86 SEA ABB=ON PLU=ON L7 AND BACTERI##
L9 7 SEA ABB=ON PLU=ON L8 AND (LYTIC OR LYS!S OR BACTERIOPHAGE)
L10 11 SEA ABB=ON PLU=ON (L1 OR (MYO OR ADENYLATE)(W)KINASE OR MYOKINASE) AND ANTIBIOT?
L11 0 SEA ABB=ON PLU=ON (L9 OR L10) NOT L6

(FILE 'MEDLINE, BIOSIS, EMBASE, WPIDS, CONFSCI, SCISEARCH, BIOTECHDS, JAPIO' ENTERED AT 10:58:10 ON 29 OCT 2001)

L12 9 S L9
L13 16 S L10
L14 24 S L12 OR L13
L15 19 DUP REM L14 (5 DUPLICATES REMOVED)

L15 ANSWER 1 OF 19 EMBASE COPYRIGHT 2001 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 2001362657 EMBASE
TITLE: Influence of phage population on the phage-mediated bioluminescent **adenylate kinase** (AK) **assay** for **detection** of **bacteria**.
AUTHOR: Wu Y.; Brovko L.; Griffiths M.W.
CORPORATE SOURCE: Dr. L. Brovko, Department of Food Science, University of Guelph, Guelph, Ont. N1G 2W1, Canada. lbrovko@uoguelph.ca
SOURCE: Letters in Applied Microbiology, (2001) 33/4 (311-315).
Refs: 12
ISSN: 0266-8254 CODEN: LAMIE7
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 004 Microbiology
LANGUAGE: English
SUMMARY LANGUAGE: English
AB Aims: The effect of phage concentration on the activity of **adenylate kinase** (AK) released from the cells lysed during infection was investigated in order to optimize a bioluminescent phage-mediated method for **bacterial**

enumeration. Methods and Results: The number of **bacteria** lysed by phages specific to Salmonella enteritidis and E. coli was **determined** using a bioluminescent method for the **detection** of AK released. In order to optimize the **assay**, the effect of phage concentration and time of infection on the amount of AK released was investigated. The release of AK was greatest at a multiplicity of infection (moi) of 10-100. Conclusions: The amount of AK released from Salmonella enteritidis and E. coli G2-2 cells by specific phages, SJ2 and AT20, respectively, depended on the type of **bacteria**, the stage of growth, the nature of phage, moi and time. Significance and Impact of the Study: An **assay** is described which allows **detection** of E. coli and Salmonella Enteritidis within 2 h at levels of 10(3) cfu ml(-1).

L15 ANSWER 2 OF 19 SCISEARCH COPYRIGHT 2001 ISI (R)
ACCESSION NUMBER: 2000:448679 SCISEARCH
THE GENUINE ARTICLE: 322ZH
TITLE: The crystal structures of chloramphenicol phosphotransferase reveal a novel inactivation mechanism
AUTHOR: Izard T (Reprint); Ellis J
CORPORATE SOURCE: ST JUDE CHILDRENS HOSP, DEPT BIOL STRUCT, 332 N LAUDERDALE ST, MEMPHIS, TN 38105 (Reprint); UNIV LEICESTER, DEPT BIOCHEM, LEICESTER LE1 7RH, LEICS, ENGLAND
COUNTRY OF AUTHOR: USA; ENGLAND
SOURCE: EMBO JOURNAL, (1 JUN 2000) Vol. 19, No. 11, pp. 2690-2700.
Publisher: OXFORD UNIV PRESS, GREAT CLARENDON ST, OXFORD OX2 6DP, ENGLAND.
ISSN: 0261-4189.
DOCUMENT TYPE: Article; Journal
FILE SEGMENT: LIFE
LANGUAGE: English
REFERENCE COUNT: 42

ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB Chloramphenicol (Cm), produced by the soil bacterium Streptomyces venezuelae, is an inhibitor of bacterial ribosomal peptidyltransferase activity. The Cm-producing streptomycete modifies the primary (C-3) hydroxyl of the **antibiotic** by a novel Cm-inactivating enzyme, chloramphenicol 3-O-phosphotransferase (CPT), Here we describe the crystal structures of CPT in the absence and presence of bound substrate. The enzyme is dimeric in a sulfate-free solution and tetramerization is induced by ammonium sulfate, the crystallization precipitant. The tetrameric quaternary structure exhibits crystallographic 222 symmetry and has ATP binding pockets located at a crystallographic 2-fold axis. Steric hindrance allows only one ATP to bind per dimer within the tetramer, In addition to active site binding by Cm, an electron-dense feature resembling the enzyme's product is found at the other subunit interface, The structures of CPT suggest that an aspartate acts as a general base to accept a proton from the 3-hydroxyl of Cm, concurrent with nucleophilic attack of the resulting oxyanion on the gamma-phosphate of ATP. Comparison between liganded and substrate-free CPT structures highlights side chain movements of the active site's Arg136 guanidinium group of >9 Angstrom upon substrate binding.

L15 ANSWER 3 OF 19 WPIDS COPYRIGHT 2001 DERWENT INFORMATION LTD
ACCESSION NUMBER: 1999-479055 [40] WPIDS
DOC. NO. CPI: C1999-140953
TITLE: Use of an **assay** for adenylate cyclase kinase in an in vitro test for the effects of external conditions on the growth of **bacterial** cells.
DERWENT CLASS: B04 D16
INVENTOR(S): MURPHY, M J; PRICE, R L; SQUIRRELL, D J; MURPHY, M; SQUIRREL, D J
PATENT ASSIGNEE(S): (MINA) UK SEC FOR DEFENCE; (MINA) UK SEC FOR DEFENCE EVALUATION & RES AGEN
COUNTRY COUNT: 85
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 9937799	A1	19990729	(199940)*	EN	36
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL OA PT SD SE SZ UG ZW					
W: AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT UA UG US UZ VN YU ZW					
AU 9920653	A	19990809	(200001)		
GB 2348702	A	20001011	(200052)		
NO 2000003708	A	20000921	(200056)		
BR 9907161	A	20001024	(200058)		
EP 1049798	A1	20001108	(200062)	EN	
R: AT BE CH DE DK ES FR GB GR IE IT LI LU NL PT SE					
CN 1294634	A	20010509	(200146)		
HU 2001001276	A2	20010828	(200157)		

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 9937799	A1	WO 1999-GB89	19990112
AU 9920653	A	AU 1999-20653	19990112
GB 2348702	A	WO 1999-GB89	19990112
		GB 2000-17298	20000717
NO 2000003708	A	WO 1999-GB89	19990112
		NO 2000-3708	20000719
BR 9907161	A	BR 1999-7161	19990112
		WO 1999-GB89	19990112
EP 1049798	A1	EP 1999-901020	19990112
		WO 1999-GB89	19990112
CN 1294634	A	CN 1999-804269	19990112
HU 2001001276	A2	WO 1999-GB89	19990112
		HU 2001-1276	19990112

FILING DETAILS:

PATENT NO	KIND		PATENT NO
AU 9920653	A	Based on	WO 9937799
GB 2348702	A	Based on	WO 9937799

BR 9907161 A Based on WO 9937799
EP 1049798 A1 Based on WO 9937799
HU 2001001276 A2 Based on WO 9937799

PRIORITY APPLN. INFO: GB 1998-16993 19980806; GB 1998-1126 19980121
AN 1999-479055 [40] WPIDS
AB WO 9937799 A UPAB: 19991004
NOVELTY - The use of an **assay** for **adenylate kinase** in an in vitro test for the effect of external conditions on the growth characteristics of **bacterial** cells, is new.
DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for:
(1) a method for **determining** the susceptibility of a **bacteria** to a reagent, comprising:
(a) **assaying** for the **adenylate kinase** released by **lysis** of **bacteria** from a culture containing the reagent; and
(b) comparing the results with those obtained from a similar **adenylate kinase assay** which is either of the culture prior to addition of reagent, and/or of lysed **bacteria** from the same culture at a different point in time and/or of lysed **bacteria** from a similar culture which does not contain the reagent;
(2) a method of **determining** the growth phase of a **bacterial** culture, comprising:
(a) subjecting a first sample of the **bacterial** culture to a **lytic** reagent so as to lyse **bacterial** cells;
(b) **assaying** for **adenylate kinase** in the first sample;
(c) **assaying** for **adenylate kinase** in a second sample of the culture which has not been exposed to the **lytic** agent; and
(d) comparing the results obtained from a first and second cultures and assessing the growth stage of the culture;
(3) a method for **determining** the sensitivity of a **bacteria** to an **antibiotic** or biostatic agent comprising:
(a) incubating a first sample of culture of **bacteria**, a second sample in the presence of **antibiotic**, a third sample in the presence of a **bacteriophage** which will specifically lyse target **bacteria** and a fourth sample in the presence of both **bacteriophage** and the **antibiotic**;
(b) **determining** the **adenylate kinase** content of each of the first to fourth samples after culture; and
(c) **determining** the sensitivity o resistivity of the **bacteria** on the basis of the **adenylate kinase assay** results and on the mode of action of the **antibiotic** or biostatic agent; and
(4) a test kit for testing the sensitivity of **bacteria** to **antibiotics**, comprising one or more **antibiotics** , and one or more reagents necessary for **assaying** for **adenylate kinase**.
USE - The test is for the sensitivity of a **bacteria**

to an **antibiotic** or biostatic agent, or to assess the growth stage of the **bacteria** (all claimed). Dwg.0/5

L15 ANSWER 4 OF 19 SCISEARCH COPYRIGHT 2001 ISI (R)
ACCESSION NUMBER: 1998:583877 SCISEARCH
THE GENUINE ARTICLE: 103TV
TITLE: Genetically engineered zinc-chelating **adenylate kinase** from Escherichia coli with enhanced thermal stability
AUTHOR: Perrier V; BurlacuMiron S; Bourgeois S; Surewicz W K; Gilles A M (Reprint)
CORPORATE SOURCE: INST PASTEUR, LAB CHIM STRUCT MACROMOL, 28 RUE DR ROUX, F-75724 PARIS 15, FRANCE (Reprint); INST PASTEUR, LAB CHIM STRUCT MACROMOL, F-75724 PARIS 15, FRANCE; INST CURIE RECH, INSERM, U350, F-91405 ORSAY, FRANCE; INST NATL AGRON PARIS GRIGNON, CTR GRIGNON, LAB SCI SOLS & HYDROL, F-78850 THIVERVAL GRIGNON, FRANCE; UNIV MISSOURI, DEPT OPHTHALMOL, COLUMBIA, MO 65212
COUNTRY OF AUTHOR: FRANCE; USA
SOURCE: JOURNAL OF BIOLOGICAL CHEMISTRY, (24 JUL 1998) Vol. 273, No. 30, pp. 19097-19101.
Publisher: AMER SOC BIOCHEMISTRY MOLECULAR BIOLOGY INC, 9650 ROCKVILLE PIKE, BETHESDA, MD 20814.
ISSN: 0021-9258.
DOCUMENT TYPE: Article; Journal
FILE SEGMENT: LIFE
LANGUAGE: English
REFERENCE COUNT: 41
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB In contrast with **adenylate kinase** from Gram-negative **bacteria**, the enzyme from Gram-positive organisms harbors a structural Zn2+ bound to 3 or 4 Cys residues in the structural motif Cys-X-2-Cys-X-16-Cys-X-2-Cys/Asp. Site-directed mutagenesis of His(126), Ser(129), Asp(146), and Thr(149) (corresponding to Cys(130), Cys(133), Cys(150), and Cys(153) in **adenylate kinase** from Bacillus stearothermophilus) in Escherichia coli **adenylate kinase** was undertaken for **determining** whether the presence of Cys residues is the only prerequisite to bind zinc or (possible) other cations. A number of variants of **adenylate kinase** from E. coli, containing 1-4 Cys residues were obtained, purified, and analyzed for metal content, structural integrity, activity, and thermodynamic stability. All mutants bearing 3 or 4 cysteine residues acquired zinc binding properties. Moreover, the quadruple mutant exhibited a remarkably high thermal stability as compared with the wild-type form with preservation of the kinetic parameters of the parent enzyme.

L15 ANSWER 5 OF 19 MEDLINE DUPLICATE 1
ACCESSION NUMBER: 1998297319 MEDLINE
DOCUMENT NUMBER: 98297319 PubMed ID: 9633663
TITLE: Specific **assays** for **bacteria** using phage mediated release of **adenylate kinase**.
AUTHOR: Blasco R; Murphy M J; Sanders M F; Squirrell D J
CORPORATE SOURCE: MAFF Central Science Laboratory, Sand Hutton, York,

UK.
SOURCE: JOURNAL OF APPLIED MICROBIOLOGY, (1998 Apr) 84 (4) 661-6.
Journal code: CT3; 9706280. ISSN: 1364-5072.
PUB. COUNTRY: ENGLAND: United Kingdom
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199807
ENTRY DATE: Entered STN: 19980716
Last Updated on STN: 19980716
Entered Medline: 19980709

AB A sensitive and rapid **assay** method for the specific **detection** of **bacteria** was developed using Escherichia coli and Salmonella newport as the test organisms. **Bacteriophages** were used to provide specific **lysis** of the **bacteria** and then the release of cell contents was measured by ATP bioluminescence. Increased sensitivity was obtained by focusing on the **bacteria**'s **adenylate kinase** (AK) as the cell marker instead of ATP as conventionally used. Fewer than 10(3) E. coli cells could be readily **detected** in less than 1 h. Salmonella newport **assays**, although as sensitive, were slower and took up to 2 h. The effects of the culture medium, the phage, and the presence of non-specific **bacteria** were examined.

L15 ANSWER 6 OF 19 SCISEARCH COPYRIGHT 2001 ISI (R)
ACCESSION NUMBER: 95:471150 SCISEARCH
THE GENUINE ARTICLE: RG310
TITLE: PRODUCT OF FOSC, A GENE FROM PSEUDOMONAS-SYRINGAE, MEDIATES FOSFOMYCIN RESISTANCE BY USING ATP AS COSUBSTRATE
AUTHOR: GARCIA P; ARCA P; SUAREZ J E (Reprint)
CORPORATE SOURCE: UNIV OVIEDO, FAC MED, AREA MICROBIOL, C JULIAN CLAVERIA SN, E-33006 OVIEDO, SPAIN (Reprint); UNIV OVIEDO, FAC MED, AREA MICROBIOL, E-33006 OVIEDO, SPAIN
COUNTRY OF AUTHOR: SPAIN
SOURCE: ANTIMICROBIAL AGENTS AND CHEMOTHERAPY, (JUL 1995) Vol. 39, No. 7, pp. 1569-1573.
ISSN: 0066-4804.
DOCUMENT TYPE: Article; Journal
FILE SEGMENT: LIFE
LANGUAGE: ENGLISH
REFERENCE COUNT: 35
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB Pseudomonas syringae PB-5123, a producer of fosfomycin, is resistant to high concentrations of the **antibiotic**. Two possible mechanisms of resistance have been detected: (i) impermeability to exogenous fosfomycin, even in the presence of sugar phosphate uptake inducers, and (ii) **antibiotic** phosphorylation. The gene responsible for this last activity, fosC, encodes a ca, 19,000-Da protein and is immediately followed by a second open reading frame, which shows sequence similarities to glutathione S-transferases. FosC uses ATP as ii cosubstrate in an inactivation reaction that can be reversed with alkaline phosphatase. Other nucleotide triphosphates cannot be substituted for ATP in this reaction. No relationship between fosC and the

previously described genes of fosfomycin resistance was found.

L15 ANSWER 7 OF 19 SCISEARCH COPYRIGHT 2001 ISI (R)
ACCESSION NUMBER: 95:132120 SCISEARCH
THE GENUINE ARTICLE: QF785
TITLE: 3 CONSERVED GLYCINE RESIDUES IN VALINE ACTIVATION OF GRAMICIDIN-S SYNTHETASE-2 FROM BACILLUS-BREVIS
AUTHOR: SAITO M (Reprint); HORI K; KUROTSU T; KANDA M; SAITO Y
CORPORATE SOURCE: HYOGO MED UNIV, DEPT BIOCHEM, MUKOGAWA CHO, NISHINOMIYA, HYOGO 663, JAPAN (Reprint)
COUNTRY OF AUTHOR: JAPAN
SOURCE: JOURNAL OF BIOCHEMISTRY, (FEB 1995) Vol. 117, No. 2, pp. 276-282.
ISSN: 0021-924X.
DOCUMENT TYPE: Article; Journal
FILE SEGMENT: LIFE
LANGUAGE: ENGLISH
REFERENCE COUNT: 44

ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB The translated product from the gene fragment containing the second and third domains of gramicidin S synthetase 2 was purified to an essentially homogeneous state, It showed valine- and ornithine-activating activity and the second domain was proved to be the valine-activating domain. Three mutant genes from Bacillus brevis Nagano, BI-3, E-4, and E-5 strains, which encode defective valine-activating domains of gramicidin S synthetase 2, were sequenced. By comparison with the wild-type gene, single point mutations of guanine to adenine were found at the three conserved glycine codons; the 5303rd guanine in BI-3, the 5378th guanine in E-4, and the 4967th guanine in E-5, which corresponded to codon changes of the 1768th glycine to glutamic acid and the 1793rd and the 1656th glycine to aspartic acid. Loss of valine-adenylation activity by mutation at the 1656th glycine proved the direct participation of the TSGT/STGXPKG motif in the adenylation reaction, and suggests that this glycine residue with the conserved lysine residue of the motif forms the phosphate-binding loop for ATP-binding, The 1793rd glycine is a member of the YGXTE motif which was also conserved among adenylate-forming enzymes except acetyl-CoA synthetases. The 1768th glycine residue appears to maintain the conformation of the active site for aminoacyl adenylation since this residue is retained among the adenylate-forming enzymes, though flanking regions are not conserved, These results suggest that these glycine residues are essential for adenylate formation in the **antibiotic** peptide synthetase family and some other adenylate-forming enzymes,

L15 ANSWER 8 OF 19 SCISEARCH COPYRIGHT 2001 ISI (R)
ACCESSION NUMBER: 94:518275 SCISEARCH
THE GENUINE ARTICLE: PD219
TITLE: ZINC CHELATION AND STRUCTURAL STABILITY OF **ADENYLATE KINASE** FROM BACILLUS-SUBTILIS
AUTHOR: PERRIER V; SUREWICZ W K; GLASER P; MARTINEAU L; CRAESCU C T; FABIAN H; MANTSCH H H; BARZU O; GILLES A M (Reprint)
CORPORATE SOURCE: INST PASTEUR, UNITE BIOCHIM REGULAT CELLULAIRES, 28 RUE DOCTEUR ROUX, F-75724 PARIS 15, FRANCE

(Reprint); INST PASTEUR, UNITE BIOCHIM REGULAT CELLULAIRES, F-75724 PARIS 15, FRANCE; MAX DELBRUCK CTR MOLEC MED, W-1115 BERLIN, GERMANY; INST PASTEUR, UNITE REGULAT EXPRESS GENET, F-75724 PARIS 15, FRANCE; INST CURIE, INSERM, U350, BIOL SECT, F-91405 ORSAY, FRANCE; NATL RES COUNCIL CANADA, INST BIOL SCI, OTTAWA K1A 0R6, ON, CANADA; NAT RES COUNCIL, INST BIODIAGNOST, WINNIPEG R3B 1Y6, MB, CANADA
COUNTRY OF AUTHOR: FRANCE; GERMANY; CANADA
SOURCE: BIOCHEMISTRY, (23 AUG 1994) Vol. 33, No. 33, pp. 9960-9967.
ISSN: 0006-2960.
DOCUMENT TYPE: Article; Journal
FILE SEGMENT: LIFE
LANGUAGE: ENGLISH
REFERENCE COUNT: 29

ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB **Adenylate kinase** from Bacillus subtilis, like the enzyme from Bacillus stearothermophilus, contains a structural zinc atom. Cys153 in the enzyme from B. stearothermophilus, which is involved in the zinc coordination, is replaced in the **adenylate kinase** from B. subtilis by an aspartic acid residue. Therefore, we were interested in establishing whether this difference has an impact on the structure, the metal chelation, and the overall stability of these proteins. We also were interested in **determining** whether His 138, which is conserved in many **adenylate kinases**, can act as a fourth partner in the metal chelation and, in general, whether His can successfully replace Cys or Asp in coordinating zinc in the **adenylate kinase** from B. subtilis. The adk gene from B. subtilis was cloned by polymerase chain reaction. The wild-type protein, together with several variants obtained by site-directed mutagenesis, were expressed in Escherichia coil and analyzed by biochemical and physicochemical methods. The H138N and D153C mutants of **adenylate kinase** from B. subtilis exhibited properties similar to those of the wild-type protein, indicating that His138 is not involved in metal coordination and that Asp153, just like Cys in the analogous position in the enzyme from B. stearothepmophilus, can participate in zinc chelation. This is the first experimental evidence indicating that aspartic acid can be involved in the coordination of a structural zinc atom. On the other hand, the D153H and D153T variants showed significant changes in their zinc-binding properties. Dialysis of the latter proteins against buffer (in both the presence and the absence of 2 mM EDTA) resulted in removal of the metal ion and loss of enzymatic activity. These mutants reacted readily with 5,5-dithiobis(2-nitrobenzoic acid) under ''native'' conditions, unlike the wild-type protein and the H138N and D153C variants of the enzyme. A fifth modified form of **adenylate kinase** from B. subtilis probed in this study, C130H, showed characteristics similar to those of the D153T mutant with respect to both metal chelation and reactivity toward 5, 5'-dithiobis(2-nitrobenzoic acid). Differences between the circular dichroism spectra of wild-type enzyme and those of the C130H mutant suggest a less compact structure of the mutant, which also explains its decreased stability against denaturation by temperature or guanidinium hydrochloride or against inactivation by trypsin. In conclusion, the zinc-chelating property of **adenylate kinase** from B. subtilis, and in general from the

Gram-positive **bacteria**, is compatible only with the presence of three or four Cys residues in the following sequence: Cys-X(2)-Cys-X(16)-Cys-X(2)-Asp/Cys.

L15 ANSWER 9 OF 19 MEDLINE
ACCESSION NUMBER: 94029011 MEDLINE
DOCUMENT NUMBER: 94029011 PubMed ID: 8215443
TITLE: Reversal of the red beet tonoplast H(+)-ATPase by a pyrophosphate-generated proton electrochemical gradient.
AUTHOR: Schmidt A L; Briskin D P
CORPORATE SOURCE: Department of Agronomy, University of Illinois, Urbana 61801.
SOURCE: ARCHIVES OF BIOCHEMISTRY AND BIOPHYSICS, (1993 Nov 1) 306 (2) 407-14.
Journal code: 6SK; 0372430. ISSN: 0003-9861.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199311
ENTRY DATE: Entered STN: 19940117
Last Updated on STN: 19970203
Entered Medline: 19931119

AB The reversal of the tonoplast H(+)-ATPase to mediate ATP synthesis was investigated in tonoplast vesicles isolated from red beet (Beta vulgaris L.) storage tissue. Our approach involved use of the H(+)-PP(i)ase to establish a proton electrochemical gradient (delta muH+) across the tonoplast vesicle membrane to drive the H(+)-ATPase in reverse. However, an initial problem with this approach was the presence of an **adenylate kinase** activity in the tonoplast fraction that interfered with measurement of ATP synthesis as a coupling between the H(+)-ATPase and H(+)-PP(i)ase. Inclusion of the **adenylate kinase** inhibitor p1p5-di(adenosine)pentaphosphate (Ap5A) in assays at 50 microM led to a complete inhibition of this activity and allowed measurement of ATP synthesis coupled to PPi hydrolysis. When measured in the presence of Ap5A, PPi-dependent ATP synthesis was blocked by Triton X-100 and inhibited by gramicidin D, imidodiphosphate, nitrate, and bafilomycin A. These results are consistent with PPi-dependent ATP synthesis occurring as a coupled process involving a delta muH+ established across the membrane. Furthermore, the observation that ATP synthesis is inhibited by inhibitors of the tonoplast H(+)-ATPase (nitrate and bafilomycin A) would suggest that this enzyme is involved in the synthetic reaction and can operate in reverse to synthesize ATP from ADP and Pi. A thermodynamic analysis of coupling between the H(+)-PP(i)ase and H(+)-ATPase suggests that PPi-driven ATP synthesis could only occur under these reaction conditions if the H+/substrate stoichiometries for the H(+)-PP(i)ase and H(+)-ATPase were 1 and 2, respectively. These values are consistent with transport stoichiometries previously determined for these enzymes in red beet tonoplast vesicles using kinetic methods.

L15 ANSWER 10 OF 19 SCISEARCH COPYRIGHT 2001 ISI (R)
ACCESSION NUMBER: 92:407645 SCISEARCH
THE GENUINE ARTICLE: JB541
TITLE: SITE-SPECIFIC MUTATIONS OF CONSERVED C-TERMINAL RESIDUES IN AMINOGLYCOSIDE 3'-PHOSPHOTRANSFERASE-II

- PHENOTYPIC AND STRUCTURAL-ANALYSIS OF MUTANT ENZYMES
AUTHOR: KOCABIYIK S (Reprint); PERLIN M H
CORPORATE SOURCE: UNIV LOUISVILLE, DEPT BIOL, LOUISVILLE, KY, 40292 (Reprint)
COUNTRY OF AUTHOR: USA
SOURCE: BIOCHEMICAL AND BIOPHYSICAL RESEARCH COMMUNICATIONS, (30 JUN 1992) Vol. 185, No. 3, pp. 925-931. ISSN: 0006-291X.
DOCUMENT TYPE: Article; Journal
FILE SEGMENT: LIFE
LANGUAGE: ENGLISH
REFERENCE COUNT: 30

L15 ANSWER 11 OF 19 EMBASE COPYRIGHT 2001 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 91092913 EMBASE
DOCUMENT NUMBER: 1991092913
TITLE: Genetic relationships among strains of Neisseria meningitidis causing disease in Italy, 1984-7.
AUTHOR: Mastrantonio P.; Congiu M.E.; Selander R.K.; Caugant D.A.
CORPORATE SOURCE: Bacteriology and Medical Mycology Laboratory, National Institute of Health, Viale Regina Elena 209, 00161 Rome, Italy
SOURCE: Epidemiology and Infection, (1991) 106/1 (143-150). ISSN: 0950-2688 CODEN: EPINEU
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 004 Microbiology
017 Public Health, Social Medicine and Epidemiology
LANGUAGE: English
SUMMARY LANGUAGE: English
AB Since 1984 a change in the epidemiological pattern of meningococcal disease in Italy has occurred with a predominance of Neisseria meningitidis of serogroup C (76%), serotype 2a and a high proportion of strains resistant to sulphonamides (71%). In order to understand better the epidemiology of the group C N. meningitidis strains responsible for the disease over the last years in Italy, we studied the genetic features of phenotypically closely related strains, by enzyme electrophoresis. The results showed that the genetic and the phenotypic characteristics of the 57 strains studied were similar, suggesting the spread of a single clone during recent years in our country. This result is in agreement with the circulation of strains typical of epidemic situations, despite the decreasing incidence of meningococcal disease in Italy.

L15 ANSWER 12 OF 19 MEDLINE
ACCESSION NUMBER: 90236906 MEDLINE
DOCUMENT NUMBER: 90236906 PubMed ID: 2139646
TITLE: Mutations in the ATP-binding domain of Escherichia coli rho factor affect transcription termination in vivo.
AUTHOR: Dombroski A J; Platt T
CORPORATE SOURCE: Department of Biochemistry, University of Rochester Medical Center, New York 14642.
CONTRACT NUMBER: GM07102 (NIGMS)
GM35658 (NIGMS)

SOURCE: JOURNAL OF BACTERIOLOGY, (1990 May) 172 (5) 2477-84.
Journal code: HH3; 2985120R. ISSN: 0021-9193.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199006
ENTRY DATE: Entered STN: 19900706
Last Updated on STN: 19900706
Entered Medline: 19900605

AB Five mutant rho proteins, representing alterations at three different locations in the Escherichia coli rho gene that affect ATP hydrolytic activity but not RNA binding, were examined in vivo for function at the rho-dependent IS2 and **bacteriophage** lambda tR1 terminators. The altered amino acids in rho are located at highly conserved residues near the beta 1 and beta 4 strands of the hydrophobic ATP-binding pocket that is structurally similar to the F1-type ATPases and **adenylate kinase**. The RNA-dependent ATPase activities of the mutant rho proteins were previously shown to range from undetectable to a twofold increase over wild-type rho in vitro. Analysis of these proteins within the environment of the cell confirmed that transcription termination in vivo is indeed related to the ability of rho factor to properly hydrolyze nucleoside triphosphates, as would be predicted from results in vitro. The relative efficiency of termination at lambda tR1, as judged by lambda N= plating efficiency and by suppression of polarity of IS2 upstream of galK, was closely linked to the level of RNA-dependent ATPase activity observed in vitro for each protein. Moreover, the termination efficiency of four of the altered rho proteins at IS2 and lambda tR1 in vivo corresponded directly to the effect of these mutations on rho function at the E. coli trp t' terminator in vitro. We conclude that **determinations** of rho function in vitro accurately reflect its behavior in intracellular termination events.

L15 ANSWER 13 OF 19 MEDLINE DUPLICATE 2

ACCESSION NUMBER: 89039250 MEDLINE
DOCUMENT NUMBER: 89039250 PubMed ID: 2846986
TITLE: Nucleotide sequence of Acinetobacter baumannii aphA-6 gene: evolutionary and functional implications of sequence homologies with nucleotide-binding proteins, kinases and other aminoglycoside-modifying enzymes.
AUTHOR: Martin P; Jullien E; Courvalin P
CORPORATE SOURCE: Unite des Agents Antibacteriens, CNRS UA 271, Paris, France.
SOURCE: MOLECULAR MICROBIOLOGY, (1988 Sep) 2 (5) 615-25.
Journal code: MOM; 8712028. ISSN: 0950-382X.
PUB. COUNTRY: ENGLAND: United Kingdom
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
OTHER SOURCE: GENBANK-X7753; GENBANK-X07753; GENBANK-XO7753
ENTRY MONTH: 198812
ENTRY DATE: Entered STN: 19900308
Last Updated on STN: 19950206
Entered Medline: 19881220

AB A new kanamycin-resistance gene, detected in Acinetobacter baumannii and designated aphA-6, was sequenced. It specifies a 30319 Dalton

3'-aminoglycoside phosphotransferase (APH(3'] that mediates resistance to kanamycin and structurally related aminoglycosides, including amikacin. Pairwise comparisons of the six types of APH(3') so far detected in human pathogens (types I, II, III and VI) and in amino-glycoside-producing microorganisms (types IV and V), confirm that APH(3') enzymes have diverged from a common ancestor. Three highly retained motifs (1: V--HGD----N; 2: G--D-GR/K-G and 3: D--K/R--Y/F---LDE) located in the C-terminal part of the enzymes were defined. Screening of protein sequence data bases fore each of these motifs revealed that motifs 1 and 2 are both found in nucleotide-binding phosphotransferases associated with a variety of biological processes, namely **adenylate kinase**, viral oncogenic protein kinases, elongation factors, Na+/K+-transporting ATPase, myosin and **antibiotic** -modifying enzymes. Motif 2 probably corresponds to the MgATP binding site, while motifs 3 and 1 could be involved in the splitting of the phosphodiester bond and in the phosphate transfer, respectively. Moreover, an additional motif, almost invariably centrally located, was found in all aminoglycoside-modifying enzymes. The occurrence of this motif, possibly a recombination site which would have allowed the association of units of separate functions, is compatible with a modular concept for the structure of aminoglycoside-modifying enzymes.

L15 ANSWER 14 OF 19 JICST-EPlus COPYRIGHT 2001 JST
ACCESSION NUMBER: 880387419 JICST-EPlus
TITLE: The enzymatic mechanisms of resistant to aminoglycoside **antibiotics** in methicillin-cephem-resistant Staphylococcus aureus.
AUTHOR: MATSUHASHI YUJI; YAMAMOTO HARUO
CORPORATE SOURCE: Meiji Seika Kaisha, Ltd., Pharmaceutical Res. Labs.
SOURCE: Jpn J Antibiot, (1988) vol. 41, no. 5, pp. 523-529. Journal Code: G0490A (Fig. 4, Tbl. 2, Ref. 21) CODEN: JJANAX; ISSN: 0368-2781
PUB. COUNTRY: Japan
DOCUMENT TYPE: Journal; Article
LANGUAGE: Japanese
STATUS: New
AB We investigated enzymatic mechanisms of resistance to aminoglycoside **antibiotics** in methicillin-cephem-resistant Staphylococcus aureus(MRSA) by elucidation of the structures of the enzymatic reaction products. According to the MIC data, MRSA, (46 strains) can be classified into 3 groups as follows. 1. Group I (35 strains) was highly resistant to gentamicin(GM) and tobramycin(TOB), and produced 2"-aminoglycosides phosphotransferase(APH (2")). 2. Group II (8 strains) was sensitive to GM, but was highly resistant to TOB, and produced 4'-aminoglycosides adenylyltransferase(AAD (4')). 3. Group III (3 strains) was sensitive to GM and TOB, but was highly resistant to kanamycin, and produced 3'-aminoglycosides phosphotransferase(APH (3'))-III. Arbekacin (HBK) was the most stable **antibiotic** to all of the inactivating-enzymes produced by MRSA, and all MRSA were sensitive to HBK.(author abst.)

L15 ANSWER 15 OF 19 MEDLINE
ACCESSION NUMBER: 82183189 MEDLINE
DOCUMENT NUMBER: 82183189 PubMed ID: 6280786
TITLE: In vitro processing of the adenosine analog formycin A to the mono-, di-, and triphosphate by a soluble

multienzyme system from mouse liver.
AUTHOR: Dye F J; Rossomando E F
CONTRACT NUMBER: DE03715 (NIDCR)
SOURCE: BIOSCIENCE REPORTS, (1982 Apr) 2 (4) 229-34.
Journal code: A6D; 8102797. ISSN: 0144-8463.
PUB. COUNTRY: ENGLAND: United Kingdom
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 198207
ENTRY DATE: Entered STN: 19900317
Last Updated on STN: 20000303
Entered Medline: 19820719

AB The adenosine kinase activity present in a soluble preparation from rat liver was investigated using formycin A (FoA), a fluorescent analog of adenosine as the phosphoryl acceptor and ATP as the donor. Reversed-phase high-performance liquid chromatography (h.p.l.c.) was used to separate substrate from product, and the progress of the phosphorylation reaction was followed by monitoring fluorometrically the amount of formycin 5'-monophosphate (FoMP), and the AMP analog, that was formed. The results showed that while FoMP was formed during the reaction indicating that an adenosine kinase activity was present, both formycin 5'-di- and triphosphate (FoDP and FoTP respectively), the corresponding analogs of ADP and ATP, were also formed, suggesting than an **adenylate kinase** activity was present. This result was confirmed with FoMP as the substrate and showing the formation of FoDP and FoTP. Other experiments carried out with FoMP as the substrate revealed the formation of FoA. Taken together, these results indicated that a 5'-nucleotidase activity as well as an **adenylate kinase** was present. Using this analog and h.p.l.c., it has been possible to demonstrate for the first time in an in vitro system the complete salvage of a nucleoside to the triphosphate level.

L15 ANSWER 16 OF 19 MEDLINE
ACCESSION NUMBER: 78171321 MEDLINE
DOCUMENT NUMBER: 78171321 PubMed ID: 649533
TITLE: Aminoglycoside resistance among Enterobacteriaceae and Acinetobacter species.
AUTHOR: Shannon K P; Phillips I; King B A
SOURCE: JOURNAL OF ANTIMICROBIAL CHEMOTHERAPY, (1978 Mar) 4 (2) 131-42.
Journal code: HD7; 7513617. ISSN: 0305-7453.
PUB. COUNTRY: ENGLAND: United Kingdom
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 197807
ENTRY DATE: Entered STN: 19900314
Last Updated on STN: 19900314
Entered Medline: 19780715

L15 ANSWER 17 OF 19 MEDLINE DUPLICATE 3
ACCESSION NUMBER: 77049893 MEDLINE
DOCUMENT NUMBER: 77049893 PubMed ID: 825418
TITLE: Regulation and biosynthesis of secondary metabolites. XVIII. Adenylate level and chlorotetracycline

production in Streptomyces aureofaciens.
AUTHOR: Curdova E; Kremen A; Vanek Z; Hostalek Z
SOURCE: FOLIA MICROBIOLOGICA, (1976) 21 (6) 481-7.
Journal code: F23; 0376757. ISSN: 0015-5632.
PUB. COUNTRY: Czechoslovakia
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 197701
ENTRY DATE: Entered STN: 19900313
Last Updated on STN: 19900313
Entered Medline: 19770129

AB The relationship was studied between the energy metabolism of the actinomycete Streptomyces aureofaciens and the biosynthesis of chlorotetracycline by this organism. The energy charge values in a culture of low-production strain were almost identical with those of a production variant but the total sum of adenylates was about 10 times higher. In the stationary growth phase both strains evinced a drop in energy charge values followed by a rise to the original level. An increase in the concentration of inorganic phosphate in fermentation medium caused a suppression of **antibiotic** formation in the lowproduction strain and further rise in the total adenylate level. The expression of the energy charge in Streptomyces aureofaciens acquires a complex character owing to the participation, apart from the adenylate system, of high-molecular polyphosphates as energy donors and the probable lack of a regulating mechanism such as the **adenylate kinase** reaction.

L15 ANSWER 18 OF 19 MEDLINE
ACCESSION NUMBER: 76119661 MEDLINE
DOCUMENT NUMBER: 76119661 PubMed ID: 2548
TITLE: Effect of sodium butyrate on mammalian cells in culture: a review.
AUTHOR: Prasad K N; Sinha P K
SOURCE: IN VITRO, (1976 Feb) 12 (2) 125-32.
Journal code: GHD; 0063733. ISSN: 0073-5655.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 197604
ENTRY DATE: Entered STN: 19900313
Last Updated on STN: 19970203
Entered Medline: 19760427

AB Sodium butyrate produces reversible changes in morphology, growth rate, and enzyme activities of several mammalian cell types in culture. Some of these changes are similar to those produced by agents which increase the intracellular level of adenosine 3',5'-cyclic monophosphate (cAMP) or by analogs of cAMP. Sodium butyrate increases the intracellular level of cAMP by about two fold in neuroblastoma cells; therefore, some of the effects of sodium butyrate on these cells may in part be mediated by cAMP. Sodium butyrate appears to have properties of a good chemotherapeutic agent for neuroblastoma tumors because the treatment of neuroblastoma cells in culture causes cell death and "differentiation"; however, it is either innocuous or produces reversible morphological and biochemical alterations in other cell types.

L15 ANSWER 19 OF 19 BIOSIS COPYRIGHT 2001 BIOSIS
ACCESSION NUMBER: 1970:193725 BIOSIS
DOCUMENT NUMBER: BA51:103725
TITLE: LIGHT INDUCED FORMATION OF ENZYMES OF THE CARBON-4 DI CARBOXYLIC-ACID PATHWAY OF PHOTOSYNTHESIS IN DETACHED LEAVES.
AUTHOR(S): GRAHAM D; HATCH M D; SLACK C R; SMILLIE R M
SOURCE: PHYTOCHEMISTRY, (1970) 9 (3), 521-532.
CODEN: PYTCAS. ISSN: 0031-9422.
FILE SEGMENT: BA; OLD
LANGUAGE: Unavailable

(FILE 'MEDLINE' ENTERED AT 11:01:54 ON 29 OCT 2001)

L16	1239	SEA	FILE=MEDLINE	ABB=ON	PLU=ON	"ADENYLATE KINASE"/CT
L17	80559	SEA	FILE=MEDLINE	ABB=ON	PLU=ON	ANTIBIOTICS/CT
L18	2	SEA	FILE=MEDLINE	ABB=ON	PLU=ON	L16 AND L17

L16	1239	SEA	FILE=MEDLINE	ABB=ON	PLU=ON	"ADENYLATE KINASE"/CT
L19	52191	SEA	FILE=MEDLINE	ABB=ON	PLU=ON	BACTERIA/CT
L20	6	SEA	FILE=MEDLINE	ABB=ON	PLU=ON	L16 AND L19

L21 8 L18 OR L20

L21 ANSWER 1 OF 8 MEDLINE
AN 1999201496 MEDLINE
TI Molecular surface sequence analysis of several E. coli enzymes and implications for existence of casein kinase-2 bacterial predecessor.
AU Torshin I
SO FRONTIERS IN BIOSCIENCE, (1999 Apr 1) 4 D394-407. Ref: 51
Journal code: CUE; 9702166. ISSN: 1093-4715.
AB Casein kinase-2 (CK2) is known as pleiotropic eukaryotic protein kinase that phosphorylates significant number of cellular proteins. Not all functions of the protein were registered up to the present time. However, it is known that this Ser/Thr-specific kinase is involved in the cell cycle progression and is essentially required for the eukaryotic cell viability. Fully automated molecular surface analysis procedure for identification of functionally significant surface residues and sequences on the base of protein spatial structure was elaborated. Using the elaborated procedure, several E. coli enzymes spatial structures and sequences were investigated. It was found that most of the casein kinase 2 potential sites found in sequences of enzymes are accessible for modification. Four of the 5 structures studied have CK2 consensus sites that may definitely influence the activity of the enzyme upon phosphorylation. Some of the potential "CK2-sites" has amino acid contents characteristic for physiological substrates of casein kinase 2 in eukaryotes. The main point of the elaborated method and the structural evidence for existence of a putative casein kinase E. coli predecessor or a protein with similar kinase activity are discussed. Physiological, biochemical, structural and evolutionary aspects of the existence of the putative predecessor are considered.

L21 ANSWER 2 OF 8 MEDLINE
AN 96213691 MEDLINE
TI Ancient divergence of long and short isoforms of adenylate kinase:

molecular evolution of the nucleoside monophosphate kinase family.
AU Fukami-Kobayashi K; Nosaka M; Nakazawa A; Go M
SO FEBS LETTERS, (1996 May 6) 385 (3) 214-20.
Journal code: EUH; 0155157. ISSN: 0014-5793.
AB Adenylate kinases (AK) from vertebrates are separated into three isoforms, AK1, AK2 and AK3, based on structure, subcellular localization and substrate specificity. AK1 is the short type with the amino acid sequence being 27 residues shorter than sequences of the long types, AK2 and AK3. A phylogenetic tree prepared for the AK isozymes and other members of the nucleoside monophosphate (NMP) kinase family shows that the divergence of long and short types occurred first and then differentiation in subcellular localization or substrate specificity took place. The first step involved a drastic change in the three-dimensional structure of the LID domain. The second step was caused mainly by smaller changes in amino acid sequences.

L21 ANSWER 3 OF 8 MEDLINE
AN 95068953 MEDLINE
TI Bioluminescent assay of bacterial intracellular AMP, ADP, and ATP with the use of a coimmobilized three-enzyme reagent (adenylate kinase, pyruvate kinase, and firefly luciferase).
AU Brovko LYu; Romanova N A; Ugarova N N
SO ANALYTICAL BIOCHEMISTRY, (1994 Aug 1) 220 (2) 410-4.
Journal code: 4NK; 0370535. ISSN: 0003-2697.
AB A three-enzyme coimmobilized system (firefly luciferase, pyruvate kinase, and adenylate kinase) was constructed for the bioluminescent assay of ATP, ADP, and AMP in bacterial cell extracts. Data for the reproducibility and sensitivity of the proposed method are presented. Detection limits were 1.5 pmol of ADP and 15 pmol of AMP in the sample. With this system, changes in adenine nucleotide concentrations in bacterial cells were measured during the actions exerted by external chemical and physical sources, such as additives to nutrient media and low-power He-Ne laser irradiation.

L21 ANSWER 4 OF 8 MEDLINE
AN 91095462 MEDLINE
TI Structural model of the nucleotide-binding conserved component of periplasmic permeases.
AU Mimura C S; Holbrook S R; Ames G F
SO PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED STATES OF AMERICA, (1991 Jan 1) 88 (1) 84-8.
Journal code: PV3; 7505876. ISSN: 0027-8424.
AB The amino acid sequences of 17 bacterial membrane proteins that are components of periplasmic permeases and function in the uptake of a variety of small molecules and ions are highly homologous to each other and contain sequence motifs characteristic of nucleotide-binding proteins. These proteins are known to bind ATP and are postulated to be the energy-coupling components of the permeases. Several medically important eukaryotic proteins, including the multidrug-resistance transporters and the protein encoded by the cystic fibrosis gene, are also homologous to this family. By multiple sequence alignment of these 17 proteins, the consensus sequence, secondary structure, and surface exposure were predicted. The secondary structural motifs that are conserved among nucleotide-binding proteins were identified in adenylate kinase, p21ras, and elongation factor Tu by superposition of their known tertiary structures. The equivalent secondary structural elements in

the predicted conserved component were located. These, together with sequence information, served as guides for alignment with adenylate kinase. A model for the structure of the ATP-binding domain of the permease proteins is proposed by analogy to the adenylate kinase structure. The characteristics of several permease mutations and biochemical data lend support to the model.

L21 ANSWER 5 OF 8 MEDLINE
AN 89265110 MEDLINE
TI Adenylate kinase bound to the chromatophore membranes of Rhodobactor spheroides G1C.
AU Koyama Y; Nakano T; Utsumi H; Yamamoto S
SO PHOTOCHEMISTRY AND PHOTOBIOLOGY, (1989 Apr) 49 (4) 501-8.
Journal code: P69; 0376425. ISSN: 0031-8655.
AB Transformation of adenylates (AMP, ADP and ATP) by washed chromatophore membranes of Rhodobactor spheroides G1C in the dark and in the light indicated the functions of ATPase (ADP + Pi in equilibrium ATP) and of an adenylate kinase (2ADP in equilibrium AMP + ATP). The activity of adenylate kinase of the chromatophores was not inhibited by AP5A, and persisted even after sonication in the presence of EDTA or CaCl2; the results suggested the presence of an adenylate kinase bound to the chromatophore membrane. In search of the enzyme, the supernatant after sonication of the chromatophores in the presence of EDTA was subjected to a molecular sieve and then to ion-exchange HPLC; a fraction with high specific adenylate kinase activity, containing a very sharp peak at 55 kDa, was isolated. Preliminary characterization indicated that it is different from the well-documented water-soluble 33 kDa adenylate kinase.

L21 ANSWER 6 OF 8 MEDLINE
AN 88295732 MEDLINE
TI Structural and functional relationships in the adenylate kinase family.
AU Schulz G E
SO COLD SPRING HARBOR SYMPOSIA ON QUANTITATIVE BIOLOGY, (1987) 52 429-39.
Journal code: DMT; 1256107. ISSN: 0091-7451.

L21 ANSWER 7 OF 8 MEDLINE
AN 78171321 MEDLINE
TI Aminoglycoside resistance among Enterobacteriaceae and Acinetobacter species.
AU Shannon K P; Phillips I; King B A
SO JOURNAL OF ANTIMICROBIAL CHEMOTHERAPY, (1978 Mar) 4 (2) 131-42.
Journal code: HD7; 7513617. ISSN: 0305-7453.

L21 ANSWER 8 OF 8 MEDLINE
AN 76119661 MEDLINE
TI Effect of sodium butyrate on mammalian cells in culture: a review.
AU Prasad K N; Sinha P K
SO IN VITRO, (1976 Feb) 12 (2) 125-32.
Journal code: GHD; 0063733. ISSN: 0073-5655.
AB Sodium butyrate produces reversible changes in morphology, growth rate, and enzyme activities of several mammalian cell types in culture. Some of these changes are similar to those produced by agents which increase the intracellular level of adenosine 3',5'-cyclic monophosphate (cAMP) or by analogs of cAMP. Sodium butyrate increases the intracellular level of cAMP by about two fold

in neuroblastoma cells; therefore, some of the effects of sodium butyrate on these cells may in part be mediated by cAMP. Sodium butyrate appears to have properties of a good chemotherapeutic agent for neuroblastoma tumors because the treatment of neuroblastoma cells in culture causes cell death and "differentiation"; however, it is either innocuous or produces reversible morphological and biochemical alterations in other cell types.

(FILE 'CAPLUS,' MEDLINE, BIOSIS, EMBASE, WPIDS, CONFSCI, SCISEARCH, JICST-EPLUS, JAPIO' ENTERED AT 11:03:34 ON 29 OCT 2001)

- Author(s)

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L22         11179 S MURPHY M?/AU
L23          6922 S PRICE R?/AU
L24           149 S SQUIRRELL D?/AU
L25            16 S L22 AND L23 AND L24
L26            28 S L22 AND (L23 OR L24)
L27            16 S L23 AND L24
L28         18206 S L22 OR L23 OR L24
L29            24 S L28 AND (L1 OR (MYO OR ADENYLATE)(W)KINASE OR MYOKINASE)
L30            38 S L25 OR L26 OR L27 OR L29
L31            22 DUP REM L30 (16 DUPLICATES REMOVED)
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L31 ANSWER 1 OF 22 CAPLUS COPYRIGHT 2001 ACS DUPLICATE 1

ACCESSION NUMBER: 2001:320121 CAPLUS
DOCUMENT NUMBER: 134:337622
TITLE: Recombinant (mutant) luciferase, cDNA encoding it, and its use in bioluminescent assays and in diagnosis of diabetes
INVENTOR(S): **Squirrell, David James; Murphy, Melenie Jane; Price, Rachel Louise** ; White, Peter John; Willey, Tara Louise
PATENT ASSIGNEE(S): Secretary of State for Defence, UK
SOURCE: PCT Int. Appl., 81 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001031028	A2	20010503	WO 2000-GB4133	20001026

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: GB 1999-25161 A 19991026
GB 2000-16744 A 20000710

AB The invention provides recombinant (mutant) luciferase enzymes which show distinctive properties compared to wild-type enzymes, a cDNA mol. encoding a synthetic recombinant luciferase, the use of said luciferase enzymes in bioluminescent assays, and kits contg. them. The invention specifically provides a recombinant protein having

luciferase activity and at least 60% similarity to a wild-type luciferase, wherein the sequence of the recombinant luciferase has a mutation at residue 357 of the wild-type luciferase from Photinus pyralis. The invention relates that the recombinant luciferase is able to emit light at a different wavelength as compared to the corresponding wild-type luciferase and/or has enhanced thermostability as compared to the corresponding wild-type luciferase. The invention also relates that in general the residue corresponding to 357 in P. pyralis luciferase is changed from an acidic amino acid to a non-acidic amino acid and preferably an uncharged polar amino acid such as tyrosine. The invention also provides various recombinant luciferase proteins that contain various mutations in residues of the wild-type luciferase from P. pyralis, Luciola mingrelica, L. cruciata, and L. lateralis. The invention further provides the cDNA sequence encoding a synthetic P. pyralis luciferase, a vector contg. said cDNA sequence, and a host cell transformed with said vectors, which can be used for the recombinant prodn. of synthetic luciferase. Finally, the invention provides use of the recombinant luciferase in a bioluminescent assay and/or in diagnosis of diabetes. Mutant luciferases in accordance with the invention can produce a large (50nm) wavelength shift in emitted light and have good thermostability. The resultant color shift can be reversed by addn. of CoA.

L31 ANSWER 2 OF 22 CAPLUS COPYRIGHT 2001 ACS DUPLICATE 2
ACCESSION NUMBER: 2000:824442 CAPLUS
DOCUMENT NUMBER: 133:360589
TITLE: Cell assay, method and reagents
INVENTOR(S): **Squirrell, David James; Murphy, Melenie Jane; Price, Rachel Louise**
PATENT ASSIGNEE(S): The Secretary of State for Defence, UK
SOURCE: PCT Int. Appl., 21 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000070082	A1	20001123	WO 2000-GB1771	20000509

W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: GB 1999-11095 A 19990513

AB A method for detecting the presence of a lysed eukaryotic cell in a sample, said method comprising: (i) adding ADP to said sample under conditions which allows the conversion of ADP to ATP by cellular **adenylate kinase**, (ii) detecting ATP in said sample and relating that to the presence of **adenylate kinase** and thus to the presence of lysed cells. The method is useful in detecting the cell lysis, for example when screening

for drugs which are required to cause lysis, for example for use in tumor therapy. However, in addn., cells may, in a preliminary step, be lysed and the contents quantitated in order to establish for example the health of condition of the cells or to detect the presence of cells in sample such as milk or urine, for diagnostic purposes.

REFERENCE COUNT: 5
REFERENCE(S):
(1) Murphy, M; WO 9937799 A 1999 CAPLUS
(2) Secr Defence; WO 9602666 A 1996 CAPLUS
(3) Secr Defence Brit; WO 9417202 A 1994 CAPLUS
(4) Secr Defence Brit; WO 9602665 A 1996 CAPLUS
(5) Yeda Res & Dev; EP 0376189 A 1990 CAPLUS

L31 ANSWER 3 OF 22 CAPLUS COPYRIGHT 2001 ACS DUPLICATE 3
ACCESSION NUMBER: 2000:291219 CAPLUS
DOCUMENT NUMBER: 132:319253
TITLE: Luciferase mutants having improved thermostability
INVENTOR(S): **Squirrell, David James; Murphy, Melenie Jane; Price, Rachel Louise** ; Lowe, Christopher Robin; White, Peter John; Tisi, Laurence Carlo; Murray, James Augustus Henry
PATENT ASSIGNEE(S): The Secretary of State for Defence, UK
SOURCE: PCT Int. Appl., 40 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000024878	A2	20000504	WO 1999-GB3538	19991026
WO 2000024878	A3	20000803		
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
AU 9963573	A1	20000515	AU 1999-63573	19991026
GB 2345913	A1	20000726	GB 1999-25162	19991026
EP 1124944	A2	20010822	EP 1999-950990	19991026
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				

PRIORITY APPLN. INFO.: GB 1998-23468 A 19981028
WO 1999-GB3538 W 19991026

AB Proteins having luciferase activity and .gtoreq.60% similarity to luciferase from Photinus pyralis, Luciola mingrelica, Luciola cruciata or Luciola lateralis, Hotaria paroula, Pyrophorus plagiophtalamus, Lampyris noctiluca, Pyrocoelia nayako or Photinus pennsylanvanica are provided. At least one amino acid residue is different from that in the corresponding wild-type sequence, comprising: (a) the amino acid residue corresponding to residue 214

in Photinus pyralis luciferase; (b) the amino acid residue corresponding to residue 232 in Photinus pyralis luciferase; (c) the amino acid residue corresponding to residue 295 in Photinus pyralis luciferase; (d) the amino acid residue corresponding to acid 14 of Photinus pyralis luciferase; (e) the amino acid residue corresponding to amino acid 35 of Photinus pyralis luciferase; (f) the amino acid residue corresponding to amino acid residue 105 of Photinus pyralis luciferase; (g) the amino acid residue corresponding to amino acid residue 234 of Photinus pyralis luciferase; (h) the amino acid residue corresponding to amino acid residue 420 of Photinus pyralis luciferase; (i) the amino acid residue corresponding to amino acid residue 310 of Photinus pyralis luciferase. The luciferase enzyme mutant has increased thermostability as compared to an enzyme having the amino acid of the corresponding wild-type luciferase.

L31 ANSWER 4 OF 22 CAPLUS COPYRIGHT 2001 ACS DUPLICATE 4
ACCESSION NUMBER: 1999:487415 CAPLUS
DOCUMENT NUMBER: 131:99528
TITLE: Antibiotic sensitivity testing
INVENTOR(S): **Murphy, Melanie Jane; Price, Rachel Louise; Squirrell, David James**
PATENT ASSIGNEE(S): The Secretary of State for Defence, UK
SOURCE: PCT Int. Appl., 36 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9937799	A1	19990729	WO 1999-GB89	19990112
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
AU 9920653	A1	19990809	AU 1999-20653	19990112
GB 2348702	A1	20001011	GB 2000-20001729	19990112
BR 9907161	A	20001024	BR 1999-7161	19990112
EP 1049798	A1	20001108	EP 1999-901020	19990112
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE				
NO 2000003708	A	20000921	NO 2000-3708	20000719

PRIORITY APPLN. INFO.:
GB 1998-1126 A 19980121
GB 1998-16993 A 19980806
WO 1999-GB89 W 19990112

AB The use of an assay for **adenylate kinase** in an in vitro test for the effect of external conditions on the growth characteristics of bacterial cells. Such tests in particular include tests for the sensitivity of a bacteria to an antibiotic or a biostatic agent, and tests to assess the growth stage and health

of the bacteria. Methods of carrying out these tests and kits for effecting them are also described and claimed.

REFERENCE COUNT: 8

REFERENCE(S):
(1) Blasco, R; J APPL MICROBIOL 1998, V84(4), P661 CAPLUS
(3) James, S; WO 9417202 A 1994 CAPLUS
(4) James, S; WO 9602665 A 1996 CAPLUS
(5) Mercian Corp; JP 04370100 A 1992 CAPLUS
(7) Secr Defence; WO 9602666 A 1996 CAPLUS
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L31 ANSWER 5 OF 22 CAPLUS COPYRIGHT 2001 ACS DUPLICATE 5

ACCESSION NUMBER: 1999:299524 CAPLUS
DOCUMENT NUMBER: 130:307540
TITLE: Production of the **adenylate kinase** free luciferase using recombinant Escherichia coli expression system
INVENTOR(S): **Squirrell, David James; Price, Rachel Louise; Murphy, Melanie Jane**
PATENT ASSIGNEE(S): The Secretary of State for Defence, UK
SOURCE: PCT Int. Appl., 15 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9922004	A1	19990506	WO 1998-GB3034	19981009
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW				
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
AU 9893600	A1	19990517	AU 1998-93600	19981009
AU 731446	B2	20010329		
EP 1025235	A1	20000809	EP 1998-946599	19981009
R: AT, BE, CH, DE, DK, ES, FR, GB, IT, LI, LU, NL, SE, PT, IE, FI				

PRIORITY APPLN. INFO.: GB 1997-22481 A 19971025
WO 1998-GB3034 W 19981009

AB **Adenylate kinase** contamination of luciferase can lead to false-pos. signals when the enzyme is used anal. A method for producing luciferase which is substantially free of **adenylate kinase** is described. In this method substitution mutations were introduced into the E. coli **adenylate kinase** gene to generate a thermolabile kinase that was unstable at .gtoreq. 37.degree.. A plasmid bearing the gene for a thermostable luciferase was then introduced into this host such that the luciferase could be produced at a temp. that is permissive to the **adenylate kinase**. The culture then was raised to a higher temp. to denature the **adenylate kinase** which was present. The method can be generally applied to the prodn. of polypeptides free of specific contaminants.

REFERENCE COUNT: 4

REFERENCE(S):
(1) Belinga, H; J Chromatogr 1995, V695(1), P33 CAPLUS
(2) Nasoff, M; US 5030563 A 1991 CAPLUS
(3) Squirrell, D; WO 9417202 A 1994 CAPLUS
(4) Squirrell, D; WO 9622376 A 1996 CAPLUS

L31 ANSWER 6 OF 22 BIOSIS COPYRIGHT 2001 BIOSIS
ACCESSION NUMBER: 1999:418243 BIOSIS
DOCUMENT NUMBER: PREV199900418243
TITLE: Cellular material detection apparatus and method.
AUTHOR(S): **Squirrell, David James (1)**
CORPORATE SOURCE: (1) Department of Medical Physics and Biomedical Engineering, Salisbury District Hospital, Salisbury UK
ASSIGNEE: The Secretary of State for Defence in her Britannic Majesty's Government
PATENT INFORMATION: US 5918259 Jun. 29, 1999
SOURCE: Official Gazette of the United States Patent and Trademark Office Patents, (Jun. 29, 1999) Vol. 1223, No. 5, pp. NO PAGINATION.
ISSN: 0098-1133.
DOCUMENT TYPE: Patent
LANGUAGE: English

L31 ANSWER 7 OF 22 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1999:496889 CAPLUS
DOCUMENT NUMBER: 132:75637
TITLE: Measurement of intracellular ATP concentrations in vivo in bacterial cells expressing Km mutants of firefly luciferase
AUTHOR(S): **Squirrell, D. J.; Murphy, M. J.; Price, R. L.**; White, P. J.
CORPORATE SOURCE: DERA, Salisbury, Wiltshire, SP4 0JQ, UK
SOURCE: Biolumin. Chemilumin., Proc. Int. Symp., 10th (1999), Meeting Date 1998, 177-180. Editor(s): Roda, Aldo. Wiley: Chichester, UK.
CODEN: 67YCAD
DOCUMENT TYPE: Conference
LANGUAGE: English
AB In this paper the authors describe variants of luciferase from the North American firefly Photinus pyralis that have been genetically engineered, with the purpose of enhancing the potential of this enzyme as an in vivo reporter of cell physiol., by altering the Km for ATP and to increase the thermostability. The authors also give exptl. results obtained from luciferase-expressing E.coli cells that show how light emission can bery rapidly respond to changes in environmental conditions.
REFERENCE COUNT: 5
REFERENCE(S):
(1) Dementieva, E; Biochemistry 1996, V61(7), P915
(2) Kajiyama, N; Biochemistry 1993, V32, P13795 CAPLUS
(3) Lundin, A; Clinical and biochemical luminescence 1982, P43
(4) Squirrell, D; GB 2301592 1998 CAPLUS
(5) White, P; Biochem J 1996, V319, P343 CAPLUS

L31 ANSWER 8 OF 22 CAPLUS COPYRIGHT 2001 ACS

ACCESSION NUMBER: 1999:496888 CAPLUS
DOCUMENT NUMBER: 132:75617
TITLE: Antibiotic sensitivity testing using bacteriophage mediated lysis and ak bioluminescence
AUTHOR(S): **Price, R. L.; Murphy, M. J.; Squirrell, D. J.**
CORPORATE SOURCE: DERA Porton Down, Salisbury, Wiltshire, SP4 0JQ, UK
SOURCE: Biolumin. Chemilumin., Proc. Int. Symp., 10th (1999), Meeting Date 1998, 173-176. Editor(s): Roda, Aldo. Wiley: Chichester, UK. CODEN: 67YCAD
DOCUMENT TYPE: Conference
LANGUAGE: English
AB A rapid method for detn. the resistance or susceptibility to antibiotics of an E. coli strain in pure culture has been demonstrated. The model system based on pure culture was used for simplicity but the authors believe that this technique could have enormous potential when fully developed.
REFERENCE COUNT: 5
REFERENCE(S):
(1) Blasco, R; Journal of Applied Microbiology 1998, V84, P661 CAPLUS
(2) Hugo, W; Pharmaceutical Microbiology 5th edition 1992
(3) Madigan, M; Brock Biology of Microorganisms 8th edition 1997
(4) Sanders, M; Bioluminescence and Chemiluminescence: Fundamentals and Applied Aspects 1994, P454 CAPLUS
(5) Squirrell, D; Bioluminescence and Chemiluminescence: Fundamentals and Applied Aspects 1994, P486 CAPLUS

L31 ANSWER 9 OF 22 BIOSIS COPYRIGHT 2001 BIOSIS
ACCESSION NUMBER: 1999:70700 BIOSIS
DOCUMENT NUMBER: PREV199900070700
TITLE: Luciferase labelling method.
AUTHOR(S): **Squirrell, D. J.; Murphy, M. J.**
CORPORATE SOURCE: Porton Down, United Kingdom
ASSIGNEE: THE SECRETARY OF STATE FOR DEFENCE IN HER BRITANNIC MAJESTY'S GOVERNMENT OF THE UNITED KINGDOM OF GREAT BRITAIN AND NORTHERN IRELAND OF DEFENCE EVALUATION & RESEARCH AGENCY
PATENT INFORMATION: US 5837465 Nov. 17, 1998
SOURCE: Official Gazette of the United States Patent and Trademark Office Patents, (Nov. 17, 1998) Vol. 1216, No. 3, pp. 2895. ISSN: 0098-1133.
DOCUMENT TYPE: Patent
LANGUAGE: English

L31 ANSWER 10 OF 22 SCISEARCH COPYRIGHT 2001 ISI (R)
ACCESSION NUMBER: 1998:697346 SCISEARCH
THE GENUINE ARTICLE: 118UA
TITLE: Intensive blood-glucose control with sulphonylureas or insulin compared with conventional treatment and risk of complications in patients with type 2

diabetes (UKPDS 33)

AUTHOR: Turner R C (Reprint); Holman R R; Cull C A; Stratton I M; Matthews D R; Frighi V; **Manley S E**; Neil A; McElroy K; Wright D; Kohner E; Fox C; Hadden D; Mehta Z; Smith A; Nugent Z; Peto R; Adlel A I; Mann J I; Bassett P A; Oakes S F; Dornan T L; Aldington S; Lipinski H; Collum R; Harrison K; MacIntyre C; Skinner S; Mortemore A; Nelson D; Cockley S; Levien S; Bodsworth L; Willox R; Biggs T; Dove S; Beattie E; Gradwell M; Staples S; Lam R; Taylor F; Leung L; Carter R D; Brownlee S M; Fisher K E; Islam K; Jelfs R; Williams P A; Williams F A; Sutton P J; Ayres A; Logie L J; Lovatt C; Evans M A; Stowell L A; Ross I; Kennedy I A; Croft D; Keen A H; Rose C; Raikou M; Fletcher A E; Bulpitt C; Battersby C; Yudkin J S; Stevens R; Stearn M R; Palmer S L; Hammersley M S; Franklin S L; Spivey R S; Levy J C; Tidy C R; Bell N J; **Steemson J**; Barrow B A; Coster R; Waring K; Nolan L; Truscott E; Walravens N; Cook L; Lampard H; Merle C; Parker P; McVittie J; Draisey I; Murchison L E; Brunt A H E; Williams M J; Pearson D W; Petrie X M P; Lean M E J; Walmsley D; Lyall F; Christie E; Church J; Thomson E; Farrow A; Stowers J M; Stowers M; McHardy K; Patterson N; Wright A D; Levi N A; Shearer A C I; Thompson R J W; Taylor G; Rayton S; Bradbury M; Glover A; SmythOsbourne A; Parkes C; Graham J; England P; Gyde S; Eagle C; Chakrabarti B; Smith J; Sherwell J; Oakley N W; Whitehead M A; Hollier G P; Pilkington T; Simpson J; Anderson M; Martin S; Kean J; Rice B; Rolland A; Nisbet J; Kohner E M; Dornhorst A; Doddridge M C; Dumskyij M; Walji S; Sharp P; Sleightholm M; Vanterpool G; Frost G; Roseblade M; Elliott S; Forrester S; Foster M; Myers K; Chapman R; Hayes J R; Henry R W; Featherston M S; Archbold G P R; Copeland M; Harper R; Richardson I; Davison H A; Alexander L; Scarpello J H B; Shiers D E; Tucker R J; Worthington J R H; Angris S; Bates A; Walton J; Teasdale M; Browne J; Stanley S; Davis B A; Strange R C; Hadden D R; Kennedy L; Atkinson A B; Bell P M; McCance D R; Rutherford J; Culbert A M; Hegan C; Tennet H; Webb N; Robinson I; Holmes J; Nesbitt S; Spathis A S; Hyer S; Nanson M E; James L M; Tyrell J M; Davis C; Strugnell P; Booth M; Petrie H; Clark D; Hulland S; Barron J L; Gould B C; Singer J; Badenoch A; McGregor M; Isenberg L; Eckert M; Alibhai K; Marriot E; Cox C; Price R; Fernandez M; Ryle A; Clarke S; Wallace G; Mehmed E; Lankester J A; Howard E; Waite A; MacFarlane S; Greenwood R H; Wilson J; Denholm M J; Temple R C; Whitfield K; Johnson F; Munroe C; Gorick S; Duckworth E; Fatman M; Rainbow S; Borthwick L; Wheatcroft D J; Seaman R J; Christie R A; Wheatcroft W; Musk P; White J; McDougal S; Bond M; Raniga P; Day J L; Doshi M J; Wilson J G; HowardWilliams J R; Humphreys H; Graham A; Hicks K; Hexman S; Bayliss P; Pledger D; Newton R W; Jung R T; Roxburgh C; Kilgallon B; Dick L; Waugh N; Kilby S; Ellingford A; Burns J; Fox C V; Holloway

M C; Coghill H M; Hein N; Fox A; Cowan W; Richard M; Quested K; Evans S J; Paisey R B; Brown N P R; Tucker A J; Paisey R; Garrett F; Hogg J; Park P; Williams K; Harvey P; Wilcocks R; Mason S; Frost J; Warren C; Rocket P; Bower L; Roland J M; Brown D J; Youens J; StantonKing K; Mungall H; Ball V; Maddison W; Donnelly D; King S; Griffin P; Smith S; Church S; Dunn G; Wilson A; Palmer K; Brown P M; Humphriss D; Davidson A J M; Rose R; Armistead L; Townsend S; Poon P; Peacock I D A; Culverwell N J C; Charlton M H; Connolly B P S; Peacock J; Barrett J; Wain J; Beeston W; King G; Hill P G; Boulton A J M; Robertson A M; Katoulis V; Olukoga A; McDonald H; Kumar S; Abouaesha F; Abuaisha B; Knowles E A; Higgins S; Booker J; Sunter J; Breislin K; Parker R; Raval P; Curwell J; Davenport H; Shawcross G; Prest A; Grey J; Cole H; Sereviratne C; Young R J; Clyne J R; Gibson M; OConnell I; Wong L M; Wilson S J; Wright K L; Wallace C; McDowell D; Burden A C; Sellen E M; Gregory R; Roshan M; Vaghela N; Burden M; Sherriff C; Mansingh S; Clarke J; Grenfell J; Tooke J E; MacLeod K; Seamark C; Rammell M; Pym C; Stockman J; Yeo C; Piper J; Leighton L; Green E; Hoyle M; Jones K; Hudson A; James A J; Shore A; Higham A; Martin B; Neil H A W; Butterfield W J H; Doll W R S; Eastman R; Ferris F R; Kurinij N; McPherson K; Mahler R F; Meade T W; Shafer G; Watkins P J; Keen H; Siegel D; Wright A D; Betteridge D J; Cohen R D; Currie D; Darbyshire J; Forrester J V; Guppy T; Johnston D G; McGuire A; Murphy M; elNahas A M; Pentecost B; Spiegelhalter D; Alberti K G M M; Denton R; Home P D; Howell S; Jarrett J R; Marks V; Marmot M; Ward J D

CORPORATE SOURCE: RADCLIFFE INFIRM, DIABET RES LABS, UKPDS GRP, WOODSTOCK RD, OXFORD OX2 6HE, ENGLAND (Reprint)

COUNTRY OF AUTHOR: ENGLAND

SOURCE: LANCET, (12 SEP 1998) Vol. 352, No. 9131, pp. 837-853.
Publisher: LANCET LTD, 42 BEDFORD SQUARE, LONDON WC1B 3SL, ENGLAND.
ISSN: 0140-6736.

DOCUMENT TYPE: Article; Journal
FILE SEGMENT: LIFE; CLIN
LANGUAGE: English
REFERENCE COUNT: 47

ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB Background Improved blood-glucose control decreases the progression of diabetic microvascular disease, but the effect on macrovascular complications is unknown. There is concern that sulphonylureas may increase cardiovascular mortality in patients with type 2 diabetes and that high insulin concentrations may enhance atheroma formation. We compared the effects of intensive blood-glucose control with either sulphonylurea or insulin and conventional treatment on the risk of microvascular and macrovascular complications in patients with type 2 diabetes in a randomised controlled trial.

Methods 3867 newly diagnosed patients with type 2 diabetes, median age 54 years (IQR 48-60 years), who after 3 months' diet

treatment had a mean of two fasting plasma glucose (FPG) concentrations of 6.1-15.0 mmol/L were randomly assigned intensive policy with a sulphonylurea (chlorpropamide, glibenclamide, or. glipizide) or with insulin, or conventional policy with diet. The aim in the intensive group was FPG less than 6 mmol/L. in the conventional group, the aim was the best achievable FPG with diet atone; drugs were added only if there were hyperglycaemic symptoms or FPG greater than 15 mmol/L. Three aggregate endpoints were used to assess differences between conventional and intensive treatment: any diabetes-related endpoint (sudden death, death from hyperglycaemia or hypoglycaemia, fatal or non-fatal myocardial infarction, angina, heart failure, stroke, renal failure, amputation [of at least one digit], vitreous haemorrhage, retinopathy requiring photocoagulation, blindness in one eye,or cataract extraction); diabetes-related death (death from myocardial infarction, stroke, peripheral vascular disease, renal disease, hyperglycaemia or hypoglycaemia, and sudden death); all-cause mortality. Single clinical endpoints and surrogate subclinical endpoints were also assessed. All analyses were by intention to treat and frequency of hypoglycaemia was also analysed by actual therapy.

Findings Over 10 years, haemoglobin A(1c) (HbA(1c)) was 7.0% (6.2-8.2) in the intensive group compared with 7.9% (6.9-8.8) in the conventional group-an 11% reduction. There was no difference in HbA(1c) among agents in the intensive group. Compared with the conventional group, the risk in the intensive group was 12% lower (95% CI 1-21, p=0.029) for any diabetes-related endpoint; 10% lower (-11 to 27, p=0.34) for any diabetes-related death; and 6% lower (-10 to 20, p=0.44) for all-cause mortality. Most of the risk reduction in the any diabetes-related aggregate endpoint was due to a 25% risk reduction (7-40, p=0.0099) in microvascular endpoints, including the need for retinal photocoagulation. There was no difference for any of the three aggregate endpoints the three intensive agents (chlorpropamide, glibenclamide, or insulin).

Patients in the intensive group had more hypoglycaemic episodes than those in the conventional group on both types of analysis (both p<0.0001). The rates of major hypoglycaemic episodes per year were 0.7% with conventional treatment, 1.0% with chlorpropamide, 1.4% with glibenclamide, and 1.8% with insulin. Weight gain was significantly higher in the intensive group (mean 2.9 kg) than in the conventional group (p<0.001), and patients assigned insulin had a greater gain in weight (4.0 kg) than those assigned chlorpropamide (2.6 kg) or glibenclamide (1.7 kg).

Interpretation Intensive blood-glucose control by either sulphonylureas or insulin substantially decreases the risk of microvascular complications, but not macrovascular disease, in patients with type 2 diabetes. None of the individual drugs had an adverse effect on cardiovascular outcomes. All intensive treatment increased the risk of hypoglycaemia.

L31 ANSWER 11 OF 22 CAPLUS COPYRIGHT 2001 ACS DUPLICATE 6
ACCESSION NUMBER: 1998:368650 CAPLUS
DOCUMENT NUMBER: 129:146444
TITLE: Specific assays for bacteria using phage mediated release of **adenylate kinase**
AUTHOR(S): Blasco, R.; **Murphy, M. J.**; Sanders, M. F.; **Squirrell, D. J.**
CORPORATE SOURCE: MAFF Central Science Laboratory, York, UK

SOURCE: J. Appl. Microbiol. (1998), 84(4), 661-666
CODEN: JAMIFK; ISSN: 1364-5072
PUBLISHER: Blackwell Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB A sensitive and rapid assay method for the specific detection of bacteria was developed using Escherichia coli and Salmonella newport as the test organisms. Bacteriophages were used to provide specific lysis of the bacteria and then the release of cell contents was measured by ATP bioluminescence. Increased sensitivity was obtained by focusing on the bacteria's **adenylate kinase** (AK) as the cell marker instead of ATP as conventionally used. Fewer than 103 E. coli cells could be readily detected in less than 1 h. Salmonella newport assays, although as sensitive, were slower and took up to 2 h. The effects of the culture medium, the phage, and the presence of non-specific bacteria were examd.

L31 ANSWER 12 OF 22 BIOSIS COPYRIGHT 2001 BIOSIS DUPLICATE 7

ACCESSION NUMBER: 2000:433471 BIOSIS
DOCUMENT NUMBER: PREV200000433471
TITLE: Luciferase and recombinant luciferase labels.
AUTHOR(S): **Price, Rachel L.; Squirrell, David J. (1); Murphy, Melenie J.**
CORPORATE SOURCE: (1) DERA Porton Down, Salisbury, Wiltshire, SP4 0JQ UK
SOURCE: Journal of Clinical Ligand Assay, (Winter, 1998) Vol. 21, No. 4, pp. 349-357. print.
ISSN: 1081-1672.
DOCUMENT TYPE: Article
LANGUAGE: English
SUMMARY LANGUAGE: English

AB Immunoassays and nucleic acid tests are indispensable in modern clinical laboratories. In this paper, we review the use of bacterial and firefly luciferases to provide bioluminescent end-points in such tests. Several very sensitive immunoassays for a variety of different analytes have been developed using this approach. We review the following: competition assays where luciferase has been labelled with haptens, assays where firefly luciferase has been biochemically coupled to adenosine triphosphate (ATP)- or luciferin-generating reactions or bacterial luciferase to FMNH2 production, and sandwich assays where bacterial and firefly luciferases have been conjugated to antibodies. Bioluminescent gene probe assays were initially subject to considerable limitations. There were problems with the use of luciferases as enzyme labels, but in the last few years these have been overcome by the development of new coupling methods and thermostable enzymes. Therefore, the full potential of bioluminescent enzymes as labels can now be realized. We also discuss areas in which the unique properties of luciferases may provide particular advantages.

L31 ANSWER 13 OF 22 CAPLUS COPYRIGHT 2001 ACS

ACCESSION NUMBER: 1997:765033 CAPLUS
DOCUMENT NUMBER: 128:86389
TITLE: The use of **adenylate kinase** for the detection and identification of low numbers of microorganisms
AUTHOR(S): **Murphy, M. J.; Squirrell, D. J.**; Sanders, M. F.; Blasco, R.

CORPORATE SOURCE: PLSD Porton Down, Salisbury, SP4 0JQ, UK
SOURCE: Biolumin. Chemilumin., Proc. Int. Symp., 9th (1997), Meeting Date 1996, 319-322. Editor(s): Hastings, J. W.; Kricka, L. J.; Stanley, P. E. Wiley: Chichester, UK.
CODEN: 65JYAO
DOCUMENT TYPE: Conference
LANGUAGE: English
AB Two approaches for the detection and identification of low nos. of microorganisms using **adenylate kinase** (AK) are presented. In the first approach, antibodies against target organisms are coupled to magnetic microbeads. When mixed with a contaminated product, the target cells are selectively removed from suspension. The beads with captured cells are then washed to remove unbound material, and a generic lysis step carried out to release AK, which is then assayed for as a measure of the presence of microorganisms. The second approach involves selective lysis of the target population by bacteriophages and subsequent AK assay. The results obtained illustrate that specific assays using AK as an end point are both quicker and more sensitive than conventional immunoassay techniques. A typical ELISA takes 2-3 h to perform and can detect 104 to 106 cells per mL. By harnessing the cells' intracellular AK as the label, there is no need for a secondary, labeled antibody in the magnetic bead immunoassay. The use of bacteriophage allows the assay to be tailored to specific applications since the phage can be chosed to be as specific or generic as required. Both techniques can detect fewer than 1000 cells in 1 to 1.5 h. They will only detect intact, viable organisms. There is some evidence that viable non-culturable cells can also be measured via their AK content.

L31 ANSWER 14 OF 22 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1997:764978 CAPLUS
DOCUMENT NUMBER: 128:86075
TITLE: Genetic engineering of firefly luciferase towards its use as a label in gene probe assays and immunoassays
AUTHOR(S): **Price, R. L.; Squirrell, D. J. ; Murphy, M. J.**; White, P. J.
CORPORATE SOURCE: PLSD, Wiltshire, SP4 0JQ, UK
SOURCE: Biolumin. Chemilumin., Proc. Int. Symp., 9th (1997), Meeting Date 1996, 220-223. Editor(s): Hastings, J. W.; Kricka, L. J.; Stanley, P. E. Wiley: Chichester, UK.
CODEN: 65JYAO
DOCUMENT TYPE: Conference
LANGUAGE: English
AB The authors report here genetic engineering of firefly luciferase towards its use as a label in gene probe assays and immunoassays.

L31 ANSWER 15 OF 22 CAPLUS COPYRIGHT 2001 ACS DUPLICATE 8
ACCESSION NUMBER: 1996:332837 CAPLUS
DOCUMENT NUMBER: 125:5083
TITLE: Luciferase labeling method
INVENTOR(S): **Squirrell, David James; Murphy, Melenie Jane**
PATENT ASSIGNEE(S): Secretary of State for Defence, UK
SOURCE: PCT Int. Appl., 16 pp.

CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9607100	A2	19960307	WO 1995-GB2038	19950830
WO 9607100	A3	19960502		
W: AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LT, LU, LV, MD, MG, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TT				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
CA 2198470	AA	19960307	CA 1995-2198470	19950830
AU 9533525	A1	19960322	AU 1995-33525	19950830
AU 697586	B2	19981008		
EP 778945	A2	19970618	EP 1995-929977	19950830
EP 778945	B1	20011004		
R: BE, CH, DE, FR, GB, IT, LI, NL, SE				
CN 1161746	A	19971008	CN 1995-195776	19950830
BR 9508652	A	19971125	BR 1995-8652	19950830
JP 10504903	T2	19980512	JP 1995-508561	19950830
ZA 9507373	A	19960520	ZA 1995-7373	19950901
US 5837465	A	19981117	US 1997-793504	19970228

PRIORITY APPLN. INFO.: GB 1994-17593 A 19940901
WO 1995-GB2038 W 19950830

AB A method is provided for conjugating luciferase to a chem. entity, particularly to a specific binding agent such as an antibody, antigen or a nucleic acid, and more particularly an antibody, comprising (a) mixing the luciferase with one or more of D-luciferin, magnesium ions and ATP and (b) performing a covalent coupling reaction between the luciferase and the binding reagent using a covalent coupling reagent wherein the amt. of D-luciferin, magnesium ions and/or ATP is sufficient to protect the luciferase activity against inhibition by the covalent coupling reagent. Preferably the step (a) is carried out by mixing the luciferase with its substrates in soln. and preferably both magnesium and ATP are present as magnesium ATP (Mg2+ATP), optionally together with D-luciferin. In a second aspect of the invention there is provided a labeled chem. entity comprising a chem. entity conjugated to active luciferase as provided by the method of the present invention. Preferably the chem. entity is a specific binding agent suitable for use in a specific binding assay, preferably being an antibody, antigen or nucleic acid. When the binding agent is a nucleic acid, it is preferably an oligonucleotide, but may be a polynucleotide or a nucleoside, and may be used as a hybridization probe or a chain extension primer, e.g. a PCR primer. Most advantageously the entity is an antibody as previous attempts to couple antibodies to luciferase have resulted in inactivity. Test kits are further provided.

L31 ANSWER 16 OF 22 CAPLUS COPYRIGHT 2001 ACS DUPLICATE 9
ACCESSION NUMBER: 1996:313742 CAPLUS
DOCUMENT NUMBER: 124:337367
TITLE: Capture assays for microorganisms

INVENTOR(S): **Squirrell, David James**
PATENT ASSIGNEE(S): Secretary of State for Defence, UK
SOURCE: PCT Int. Appl., 26 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9602666	A1	19960201	WO 1995-GB1643	19950712
W: AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LT, LU, LV, MD, MG, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TT				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
CA 2194458	AA	19960201	CA 1995-2194458	19950712
AU 9529319	A1	19960216	AU 1995-29319	19950712
AU 691940	B2	19980528		
GB 2304892	A1	19970326	GB 1997-603	19950712
GB 2304892	B2	19980819		
EP 774011	A1	19970521	EP 1995-925048	19950712
EP 774011	B1	19990901		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, NL, PT, SE				
CN 1157638	A	19970820	CN 1995-194994	19950712
HU 76447	A2	19970929	HU 1997-90	19950712
JP 10502815	T2	19980317	JP 1995-504796	19950712
BR 9508392	A	19980526	BR 1995-8392	19950712
AT 184054	E	19990915	AT 1995-925048	19950712
ES 2136866	T3	19991201	ES 1995-925048	19950712
ZA 9505846	A	19960219	ZA 1995-5846	19950713
US 5798214	A	19980825	US 1997-765063	19970106
NO 9700106	A	19970313	NO 1997-106	19970110
PRIORITY APPLN. INFO.:			GB 1994-14096	19940713
			WO 1995-GB1643	19950712

AB A method is provided for detg. the presence and/or amt. of a microorganism and/or its intracellular material present in a sample characterized in that: (1) exposing the sample to a specific binding agent that has been immobilized upon a solid substrate, the specific binding agent being capable of binding to the microorganism or its intracellular material such that it becomes assocd. with the solid substrate. (B) exposing the solid substrate to an agent capable of making **adenylate kinase** assocd. with the microorganism and/or its intracellular material accessible to solns. applied to the substrate, (c) applying a soln. contg. ADP to the substrate under conditions whereby ATP may be produced by any **adenylate kinase** present, and (d) measuring the amt. of ATP and relating that to the presence and/or amt. of microorganism or intracellular contents. Step (d) may be carried out using an assay that includes a color forming reaction, but is preferably carried out by use of luciferase/luciferin reagent to produce light proportional to the amt. of ATP produced, and that is detected using a luminometer. Preferably step (c) includes presence of magnesium ions at a molar concn. sufficient to allow maximal conversion of ADP to ATP. Most preferably step (b) and (c) are

carried out by adding extractant, ADP and magnesium ions to the sample and incubating the mixt. for a predetd. period to effect conversion of ADP to ATP.

L31 ANSWER 17 OF 22 CAPLUS COPYRIGHT 2001 ACS DUPLICATE 10
ACCESSION NUMBER: 1996:313741 CAPLUS
DOCUMENT NUMBER: 124:336655
TITLE: Microbiological test method and reagents
INVENTOR(S): **Squirrell, David James**
PATENT ASSIGNEE(S): United Kingdom Secretary of State for Defence, London, UK
SOURCE: PCT Int. Appl., 32 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9602665	A1	19960201	WO 1994-GB1513	19940713
W: AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, ES, FI, GB, GE, HU, JP, KE, KG, KR, KZ, LK, LT, LU, LV, MD, MG, MN, MW, NL, NO, NZ, PL, PT, RO, RU, SD, SE, SI, SK, TJ, TT, UA, US, UZ, VN				
RW: KE, MW, SD, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
AU 9471305	A1	19960216	AU 1994-71305	19940713
AU 698916	B2	19981112		
GB 2303919	A1	19970305	GB 1996-27142	19940713
GB 2303919	B2	19980826		
EP 788553	A1	19970813	EP 1994-920556	19940713
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, NL, PT, SE				
CN 1164259	A	19971105	CN 1994-195171	19940713
BR 9408598	A	19971118	BR 1994-8598	19940713
NO 9700105	A	19970313	NO 1997-105	19970110
PRIORITY APPLN. INFO.:			WO 1994-GB1513	19940713

AB A method for detg. the presence and/or amt. of microorganisms and/or their intracellular material present in a sample comprising estg. the amt. of **adenylate kinase** therein by its ability to convert ADP to ATP in the presence of added magnesium ions and relating that to the presence/or amt. or organism and/or intracellular material. The method provides improved sensitivity over existing luciferase/luciferin assays. Reagents including purified ADP and **adenylate kinase** free luciferase are provided together with test kits including these and app. for automated operation of the method.

L31 ANSWER 18 OF 22 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1995:943660 CAPLUS
DOCUMENT NUMBER: 123:332582
TITLE: Cellular material detection apparatus and method
INVENTOR(S): **Squirrell, David James**
PATENT ASSIGNEE(S): United Kingdom Secretary of State for Defence, London, UK
SOURCE: PCT Int. Appl., 32 pp.

CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9525811	A1	19950928	WO 1995-GB544	19950313
W: AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, JP, KE, KG, KP, KR, KZ, LK, LR, LT, LU, LV, MD, MG, MN, MW, MX, NL, NO, NZ, PL, PT, RO, RU, SD, SE, SI, SK, TJ, TT, UA, US				
RW: KE, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
CA 2195956	AA	19950928	CA 1995-2195956	19950313
AU 9518588	A1	19951009	AU 1995-18588	19950313
AU 699575	B2	19981210		
EP 789778	A1	19970820	EP 1995-910682	19950313
EP 789778	B1	20010530		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, NL, PT, SE				
RU 2142016	C1	19991127	RU 1997-106556	19950313
ES 2156937	T3	20010801	ES 1995-910682	19950313
US 5773710	A	19980630	US 1997-793011	19970205
US 5918259	A	19990629	US 1998-63368	19980421

PRIORITY APPLN. INFO.:
GB 1994-5392 A 19940318
WO 1995-GB544 W 19950313
US 1997-793011 A3 19970205

AB A method and app. for monitoring a gaseous environment for the presence of cellular material; more particularly an app. and method that is capable of providing a measure of presence and/or nos. of cellular microorganisms, such as bacterial cells, in a large vol. of air such as in a warehouse or prodn. facility or in an open air location where bacterial presence is suspected. The method and app. of the invention are particularly provided for detg. the likelihood of pathogenic material being present in an environment by batch or online measurement of cell nos. In the latter format, a continuous monitoring of an environment for presence of pathogens is effected. The app. comprises a continuous flow luminometer preferably fed by a cyclone or high velocity virtual impactor and lytic and luminescence reagents which detect the amt. of ATP or **adenylate kinase** present in a sample of air.

L31 ANSWER 19 OF 22 CAPLUS COPYRIGHT 2001 ACS DUPLICATE 11
ACCESSION NUMBER: 1994:625854 CAPLUS
DOCUMENT NUMBER: 121:225854
TITLE: Microbiological test method and reagents
INVENTOR(S): **Squirrell, David James**
PATENT ASSIGNEE(S): United Kingdom Secretary of State for Defence, London, UK
SOURCE: PCT Int. Appl., 23 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9417202	A1	19940804	WO 1994-GB118	19940121
W: AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, ES, FI, GB, HU, JP, KP, KR, KZ, LK, LU, MG, MN, MW, NL, NO, NZ, PL, PT, RO, RU, SD, SE, SK, UA, US, VN				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
CA 2154462	AA	19940804	CA 1994-2154462	19940121
AU 9458417	A1	19940815	AU 1994-58417	19940121
AU 677627	B2	19970501		
EP 680515	A1	19951108	EP 1994-904295	19940121
EP 680515	B1	19980826		
R: AT, BE, CH, DE, DK, ES, FR, GB, IE, IT, LI, NL, PT, SE				
BR 9406417	A	19951226	BR 1994-6417	19940121
CN 1119029	A	19960320	CN 1994-191434	19940121
CN 1061378	B	20010131		
HU 72396	A2	19960429	HU 1995-2220	19940121
HU 218156	B	20000628		
AT 170222	E	19980915	AT 1994-904295	19940121
ES 2120006	T3	19981016	ES 1994-904295	19940121
CA 2194457	AA	19960201	CA 1994-2194457	19940713
NO 9502917	A	19950906	NO 1995-2917	19950721
GB 2289945	A1	19951206	GB 1995-15786	19950727
GB 2289945	B2	19970618		
US 5648232	A	19970715	US 1996-634222	19960418

PRIORITY APPLN. INFO.:		
GB 1993-1118	A	19930121
WO 1994-GB118	W	19940121
US 1995-407889	B1	19950321

AB A method for detg. the presence and/or amt. of microorganisms and/or their intracellular material present in a sample comprises estg. the amt. of **adenylate kinase** therein by its ability to convert ADP to ATP and relating that to the presence/or amt. of organism and/or intracellular material. The method provides improved sensitivity over existing luciferase/luciferin assays. Reagents including purified ADP and adenyl kinase free-luciferase are provided together with test kits including these and app. for automated operation of the method. Escherichia coli was assayed using purified ADP and the luciferase/luciferin system.

L31 ANSWER 20 OF 22 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1996:316426 CAPLUS
DOCUMENT NUMBER: 125:52710
TITLE: **Adenylate kinase** as a cell marker in bioluminescent assays
AUTHOR(S): **Squirrell, D. J.; Murphy, M. J.**
CORPORATE SOURCE: Chemical and Biological Defence Establishment, Wiltshire, SP4 0JQ, UK
SOURCE: Biolumin. Chemilumin., Proc. Int. Symp., 8th (1994), 486-489. Editor(s): Campbell, Andrew Keith; Kricka, Larry J.; Stanley, Philip E. Wiley: Chichester, UK.
CODEN: 62UZAR
DOCUMENT TYPE: Conference
LANGUAGE: English
AB From the turnover no. and the cellular ratio of **adenylate**

kinase (AK) to ATP, it would be predicted that, with a 1-min incubation, 40-50-fold as much ATP would be available for bioluminescent detection than in assays for ATP per se. Using Escherichia coli, a limit of detection of 10-100 cells could be achieved.

L31 ANSWER 21 OF 22 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1996:316387 CAPLUS
DOCUMENT NUMBER: 125:4188
TITLE: Covalent coupling of firefly luciferase to antibodies
AUTHOR(S): **Murphy, M. J.; Squirrell, D. J.**
CORPORATE SOURCE: Chemical and Biological Defence Establishment, Salisbury/Wiltshire, SP4 0JQ, UK
SOURCE: Biolumin. Chemilumin., Proc. Int. Symp., 8th (1994), 301-304. Editor(s): Campbell, Andrew Keith; Kricka, Larry J.; Stanley, Philip E. Wiley: Chichester, UK.
CODEN: 62UZAR
DOCUMENT TYPE: Conference
LANGUAGE: English
AB D-Luciferin or MgATP were used as substrate to protect the active-site thiols of firefly luciferase from inhibition during the prodn. of conjugates with IgG via the heterobifunctional crosslinking reagent sulfo-SMCC for use in immunoassay.

L31 ANSWER 22 OF 22 MEDLINE DUPLICATE 12
ACCESSION NUMBER: 86111725 MEDLINE
DOCUMENT NUMBER: 86111725 PubMed ID: 4086487
TITLE: Effects of ionic strength and sulfhydryl reagents on the binding of creatine phosphokinase to heart mitochondrial inner membranes.
AUTHOR: Wenger W C; **Murphy M P**; Brierley G P; Altschuld R A
CONTRACT NUMBER: HL23166 (NHLBI)
SOURCE: JOURNAL OF BIOENERGETICS AND BIOMEMBRANES, (1985 Oct) 17 (5) 295-303.
Journal code: HIO; 7701859. ISSN: 0145-479X.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 198603
ENTRY DATE: Entered STN: 19900321
Last Updated on STN: 19970203
Entered Medline: 19860326
AB The concept that creatine phosphokinase is bound to the outer surface of the heart mitochondrial inner membrane originated from observations that the enzyme is retained by water-swollen heart mitochondria and by digitonin-treated heart mitochondria suspended in isotonic sucrose. The present study establishes that digitonin-treated mitochondria release creatine phosphokinase in isotonic KCl, and other investigators have reported an identical response for the water-swollen organelles. These observations suggest that mitochondrial creatine phosphokinase is not bound to the outer surface of the inner membrane at a site adjacent to the adenine nucleotide translocase under physiologic conditions.